PARTICULATE MATTER AND SULFATE:
EVALUATION OF CURRENT CALIFORNIA AIR QUALITY STANDARDS
WITH RESPECT TO PROTECTION OF CHILDREN

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A. Abstract

Epidemiological evidence indicates that present-day ambient particulate matter (PM) and/or sulfate air pollution exposures are associated with adverse health effects in children, including that:

Short-term PM and/or sulfate exposures to children are associated with:

- reduced pulmonary function;

- increased respiratory symptoms in asthmatics (e.g., asthma attacks) and non-asthmatics;

- increased incidence of respiratory doctor's visits;

- increased incidence of emergency department (ED) visits and hospital admissions (HA's);

- increased mortality, and;

- especially increased infant morbidity and mortality;

Long-term chronic PM and/or sulfate exposures to children are associated with:

- reduced lung function;

- increased respiratory symptoms; and,

- increased infant mortality, intrauterine growth reduction, or pre-term delivery.

Especially apparent in the many studies examined, and of notable concern, are results indicating much higher risks for children in the neonatal (< 1 month) and post-neonatal (1-12 months) age groups. Furthermore, an examination of key medical visits and hospital admissions studies indicates that the existing Federal and California PM_{10} and $PM_{2.5}$ mass and sulfate ambient air quality standards are not presently sufficiently protective of public health, as significant adverse health impacts have been documented in published studies at mean ambient levels below these standards.

Both biological and physical exposure-related factors enhance the risk to children from PM and sulfate exposures. These risk-enhancing factors include:

- higher PM concentration exposures resulting from children's greater activity levels;

- larger PM doses in children from increased ventilation rates;

- greater doses of ultrafines among children 14-18 years of age;

- enhanced PM doses in children, especially infants, per body weight and lung surface area;

- diminished and developing defense systems in infants;

- higher prevalence of children with asthma than in other age groups;

- larger percentage of children made susceptible by poverty than other age groups; and,

- gas-particle interactions and particle-allergen interactions, potentially making the individual pollutant standards not fully protective to susceptible populations, such as children.

Based on the above insights, it is recommended that future PM research should focus on:

- improved identification of the specific characteristics of PM (e.g., ultrafines, acidity, elemental composition, etc.) that are contributing most to noted PM effects, and quantification of their relative roles in PM toxicity;

- further investigation as to whether acute exposures less than one day in length (e.g., 1-hr. daily maximum), or longer multi-day exposures (e.g., 2 or more day average PM), also have health importance, over and above that captured by the 24-hr. PM peak PM concentration measurement;

- further investigations into particle-gas and particle-allergen interactions;

- using both experimental and epidemiological methods, conduct further investigations of apparently larger acute and long-term effects of PM on children, and especially infants.

B. Background

This section briefly summarizes the existing California state and federal ambient standards for particulate matter (PM) and sulfate ($SO_4^=$), and the rationale for these standards.

According to California State Code of Regulations Section 39606 (b), the state board shall adopt standards of ambient air quality for each air basin in consideration of the public health, safety, and welfare, including, but not limited to, health, illness, irritation to the senses, aesthetic value, interference with visibility, and effects on the economy. These standards may vary from one air basin to another. Standards relating to health effects are to be based upon the recommendations of the State Department of Health Services. The term "Ambient air quality standards" means specified concentrations and exposure durations of air pollutants that reflect the relationship between the intensity and composition of air pollution to undesirable effects established by the state board or, where applicable, by the federal government. "Air contaminant" or "air pollutant" means any discharge, release, or other propagation into the atmosphere and includes, but is not limited to, smoke, charred paper, dust, soot, grime, carbon, fumes, gases, odors, particulate matter, acids, or any combination thereof.

The present particulate matter (PM) mass-based ambient air quality standard in California is indexed to PM_{10}, which refers to atmospheric particles, solid and liquid, except uncombined water, as measured by a PM_{10} sampler that collects 50 percent of all particles of 10 micrometers (um) aerodynamic diameter, and that collects a declining fraction of particles as their diameter increases and an increasing fraction of particles as their diameter decreases, reflecting the characteristic of lung deposition. Suspended particulate matter (PM_{10}) is to be measured by the size selective inlet high volume (SSI) PM_{10} sampler method in accordance with ARB Method P, as adopted on August 22, 1985, or by an equivalent PM_{10} sampler method, for purposes of monitoring for compliance with the PM_{10} standards.

As noted in Table 1, the State of California, unlike the Federal government, also has an air quality standard that was promulgated in the 1970s for the sulfate portion of PM_{10}. Sulfates are the water soluble fraction of suspended particulate matter containing the sulfate radical

($SO_4^=$) including, but not limited to, strong acids and sulfate salts, as measured by AIHL Method No. 61 (Turbidimetric Barium Sulfate) (December 1974, as revised April 1975 and February 1976) or equivalent method. The present sulfate standard is a 24-hour average concentration not to be exceeded more than once per year. In recognition of an inability to discern a threshold at and below which no effects can occur from exposure to this pollutant, this standard is set at a "Critical Harm" level.

Currently, most of the state is in non-attainment with the PM10 standard. The PM_{10} air quality levels dropped from a statewide average of approximately 80 ug/m^3 in 1988 to about 50 ug/m^3 in 1995 and 1996, but rose again to almost 60 ug/m^3 in 1997 (CARB, 1999). State average annual maximum sulfate concentrations dropped by about half between 1980 and 1990 (from about 60 ug/m^3 to about 30 ug/m^3), and have remained fairly stable since that time. Peak summer sulfate in the LA Basin in 1996 was about 17 ug/m^3, and for the last 10 years the mean summer 24-hour concentrations were less than 8 ug/m^3. Thus, typical concentrations are now below the existing sulfate standard, but this is not the case for PM_{10}.

The United States Environmental Protection Agency ("EPA") also recognized the adverse health effects of small particulate pollution as early as 1987 when, pursuant to its authority under the Clean Air Act, it promulgated a National Ambient Air Quality Standard ("NAAQS") for particulate matter that is 10 micrometers in diameter or smaller (PM_{10}). The NAAQS promulgated by EPA are required for certain air pollutants "that may reasonably be anticipated to endanger public health and welfare." The NAAQS' air criteria must be "requisite to protect the public health" with an "adequate margin of safety." Under the particulate matter NAAQS, states must reduce PM_{10} concentrations in their ambient atmosphere to no more than 50 micrograms per cubic meter on an annual average basis, and to no more than 150 micrograms per cubic meter on an average 24-hour period. Prior to 1987, EPA's particulate NAAQS had only regulated total suspended particulate matter. Its focus in 1987 on smaller particles -- that is, 10 micrometers or less -- resulted from increasing scientific evidence that human inhalation of smaller particles had more serious respiratory effects than larger particles.

Table 1. Present California Ambient Air Quality Standards for Particulate Matter and Sulfates (Source: California State Code of Regulations)				
Substance	Concentration and Methods	Duration of Averaging Periods	Most Relevant Effects	Comments
Suspended Particulate Matter (PM_{10})	50 ug/m^3 PM_{10} 30 ug/m^3 PM_{10}	24 hour sample Annual Geometric Mean of 24 hr. Samples	Prevention of excess deaths from short-term exposures and of exacerbation of symptoms in sensitive patients with respiratory disease. Prevention of excess seasonal declines in pulmonary function, especially in children	The standard applies to suspended particulate matter as collected by a PM_{10} sampler, which collects 50% of all particles of 10 um aerodynamic diameter and collects a decreasing fraction of particles as diameter increases, and an increasing fraction as their diameter decreases, reflecting the characteristics of lung deposition.
Sulfates	25 ug/m^3 Total Sulfates AIHL #61 (Turbidimetric Barium Sulfates)	24 hour sample	a. Decreases in ventilatory function b. aggravation of asthmatic symptoms c. Aggravation of cardio-pulmonary diseases d. Vegetative Damage e. Degradation of visibility f. Property damage.	This standard is based as a Critical Harm Level, not a threshold value.

In 1994, the EPA began the process of re-reviewing its particulate matter standards. In 1996, the EPA proposed a new NAAQS for even smaller particles -- those that are 2.5 micrometers in diameter or smaller ($PM_{2.5}$). This new proposed standard was based on an increasing scientific consensus that the current NAAQS for PM_{10} was not sufficiently protective of human health. EPA's scientific review concluded that fine particles, in the 2.5 micrometer and smaller range, penetrate more deeply into the lungs, and may be more likely than coarse particles to contribute to the health effects (e.g., premature mortality and hospital admissions) found in a number of recently published community epidemiological studies at concentrations that extend well below those allowed by the current U.S. PM_{10} standards. As EPA stated in its proposed regulation, a greatly expanded body of community epidemiological studies provide "evidence that serious health effects (mortality, exacerbation of chronic disease, increased hospital admissions, etc.) are associated with exposures to ambient levels of PM, even in concentrations below current U.S. PM standard" (*Federal Register*, July 18, 1997, Vol. 62, No. 138, pg. 38655).

The recently promulgated NAAQS for $PM_{2.5}$ is 15 micrograms per meter cubed (ug/m^3) based upon the 3-year average of annual arithmetic mean $PM_{2.5}$ concentrations at multiple

sites, and 65 ug/m^3 based upon the 3-year average of the 98th percentile of the 24-hour PM$_{10}$ concentration at individual sites. These standards are presently being contested in Federal courts (See: American Trucking Associations, Inc. v. USEPA, 175 F.3d 1027 (D.C. Cir. 1999), modified, 190 F.3d 4 (D.C. Cir. 1999), cert. granted in Browner v. American Trucking Associations, 120 S. Ct. 2003 (2000) (No. 99-1257), and in American Trucking Associations v. Browner, 120 S. Ct. 2193 (2000) (No. 99-1426)).

C. Factors in Particulate Matter (PM) and Sulfate Exposure and Dose Assessment

This section includes, to the extent that information is available, a description of exposure patterns among infants and children that are likely to result in disproportionately high exposures to ambient air pollutants in comparison to the general population.

C.1. PM Concentration Exposures from Children's Activities

Personal activities, such as exercise, cigarette smoking, hobbies, and occupational tasks generate a plume of particles that surround the person generating the particles. Such personal activity sources can exist either indoors or outdoors. These are microscale PM generating activities that primarily influence the exposure of the person performing the activity. Thus, personal activity PM exposure is only measured by a personal monitor carried by the subject, because a stationary monitor located nearby will not measure the high PM concentration generated by that activity. The difference between a personal monitor measurement and an area-representative measurement several meters away is sometimes called a "personal cloud" (Wallace, 1999).

However, personal PM exposure monitoring studies have indicated that personal activities, along with PM generated by personal and indoor sources (e.g., cigarette smoking), can lead to PM indoors and personal exposures to total PM that exceed the concentration of the PM found in the immediate outdoor air or in the local ambient air (Binder et al., 1976; Repace and Lowrey, 1980; Spengler et al., 1980). Fine particles have been found to readily penetrate buildings, but indoor activity adds incrementally to outdoor levels and, frequently, somewhat

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higher levels of fine particles are observed indoors. Indeed, human activity, such as smoking and cooking, does generate fine particles (<2.5 um); cooking, dusting, vacuuming and general activity can generate coarser particles (>2.5 um), or can resuspend coarse particles that previously had settled out (Litzistorf et al., 1985; Thatcher and Layton, 1995; Abt et al., 1999, 2000).

Children are well documented to have greater activity levels than adults, and therefore are likely to have increased personal exposures, relative to adults, because of an enhanced personal cloud of particles. In recent surveys of the activity patterns of California children and adults (Wiley et al, 1991a,b), it was found that children 11 years of age and under spend an average of 124 minutes/day doing active sports, walking/hiking, or outdoor recreation, vs. only 21 minutes for adults. In personal exposure studies in the Netherlands, it has been found that, given roughly the same outdoor concentrations, children have a much higher personal PM_{10} exposure than adults (Janssen, et al. 1997, 1998). While children's homes in these studies had a mean outdoor concentration similar to that of adults (41.5 ug/m^3 vs. 38.5 ug/m^3 for adults), children's personal exposures averaged 66.8 ug/m^3 above ambient vs. 26.9 ug/m^3 above ambient for adults. This indicates a much higher "personal cloud" for children than adults. In regressions, personal activity was one of the more important contributors to the children's extra personal exposure concentration, contributing approximately 12 ug/m^3. The children's personal exposure was also some 43 ug/m^3 higher than their time-weighted average of indoor and outdoor concentrations, indicating most of the personal vs. outdoor PM_{10} difference to be due to their personal cloud, rather than generally higher PM_{10} concentrations indoors. Most of these particles are likely to be of indoor origins, however. Thus, PM exposure of a child can be substantially higher than that for adults because of the extra PM that is generated by their own increased activity levels, but the importance of this effect to outdoor air pollution standard setting is limited by the fact that most of these activity generated particles are of indoor origins.

For sulfates, the "personal cloud" phenomenon apparently does not apply as it does for PM mass in general, as sulfate is derived almost exclusively from the outdoors. Indeed, in the

PTEAM study (Ozkaynak et al, 1996) conducted in Riverside, CA in 1990, it was found that

sulfate concentrations indoors and outdoors were the same, and the researchers concluded that

there appeared to be no indoor or personal sources of exposure to sulfate particles. As shown

in Figure 1, $SO_4^=$ measured at central monitoring stations in the PTEAM study is closely

correlated with $SO_4^=$ as measured by personal exposure monitors. In that figure, the deviations

from the line of identity can be largely accounted for by a model that incorporates other known

influences. Such close correspondence between personal and outdoor concentrations was not

seen for PM_{10} or $PM_{2.5}$ mass concentrations, or for other measured constituents. The close

correspondence for $SO_4^=$ can be attributed to it being: a) chemically and physically stable in the

air and on sampling filters; b) present primarily as submicrometer-sized particles which

penetrate into indoor spaces efficiently with infiltrating air; c) a secondary aerosol that is

distributed quite uniformly across large geographic areas; and d) without common indoor
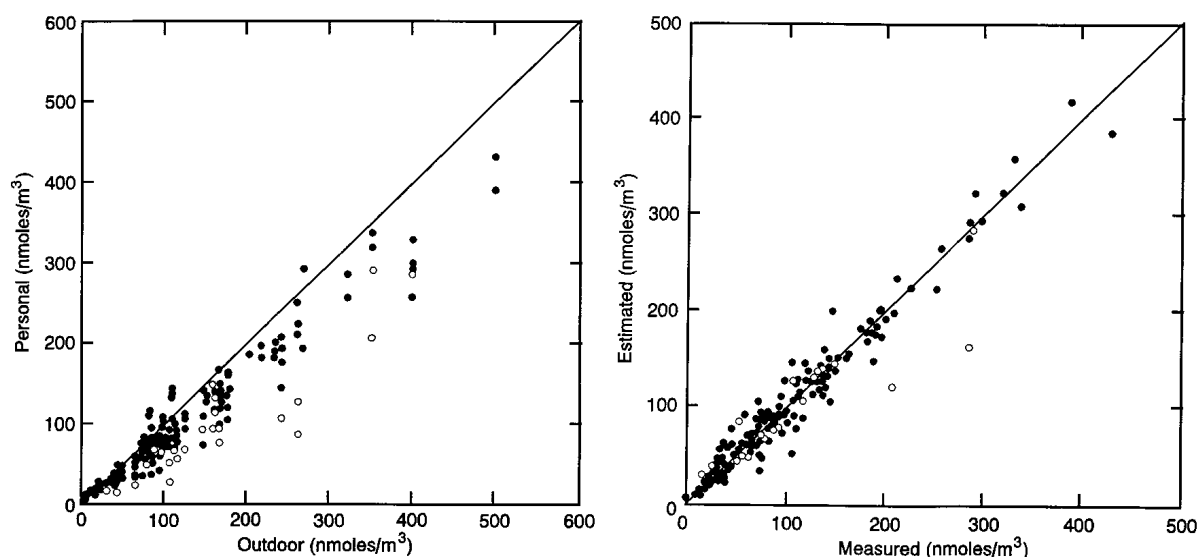
sources.

Figure 1. Left Panel: Comparison of personal monitoring data on $SO_4^=$ concentration with temporally coincident central monitoring station $SO_4^=$ in California. (Open circles are air-conditioned residences.)
Right panel: Comparison of measured ambient $SO_4^=$ concentrations with estimated personal $SO_4^=$ exposures based on PTEAM model incorporating known influences on personal exposures.
From: U.S. EPA (1995).

Thus, unlike for PM_{10}, children's personal concentration exposures to sulfates are similar

to those of adults, and are well represented by a central site monitors. However, the acidity of

sulfates has been found to differ indoors and outdoors, with diminished acidity indoors due to ammonia sources indoors that can convert the acidic sulfates to ammonium sulfate (e.g., see Suh et al, 1994). Thus, while total sulfate exposures are similar for adults and children, the sulfates that children are exposed to are likely more acidic as a result of their greater time spent outdoors, as sulfates are more likely to be in an acidic form outdoors (i.e., as sulfuric acid and/or ammonium bisulfate). Therefore, the greater outdoor time and activity of children outdoors places them at greater risk than adults of exposure to acidic sulfates and acidic gases (e.g., nitric acid).

C.2. Variations in Lung Deposition Fraction in Children vs. Adults

Lung and airway characteristics vary with age, and these variations can change the deposition pattern of inhaled particles. The limited experimental studies available indicate results ranging from no clear dependence of total deposition on age to slightly higher deposition in children than in adults. Potential deposition differences between children and adults have been assessed to a greater extent using mathematical models, as shown in Figure 2, as derived from the ICRP model (U.S. EPA, 1995). These results indicate that extra-thoracic (ET) deposition (i.e., to the nose, naso-oropharyngeal passages, and larynx) in children is generally higher than in adults, but that tracheo-bronchiolar (TB) and alveolar (A) regional deposition in children may be either higher or lower than the adult, depending upon particle size and age of the child. Overall, available studies do not provide clear evidence for significant differences in deposition fraction between adults and children.
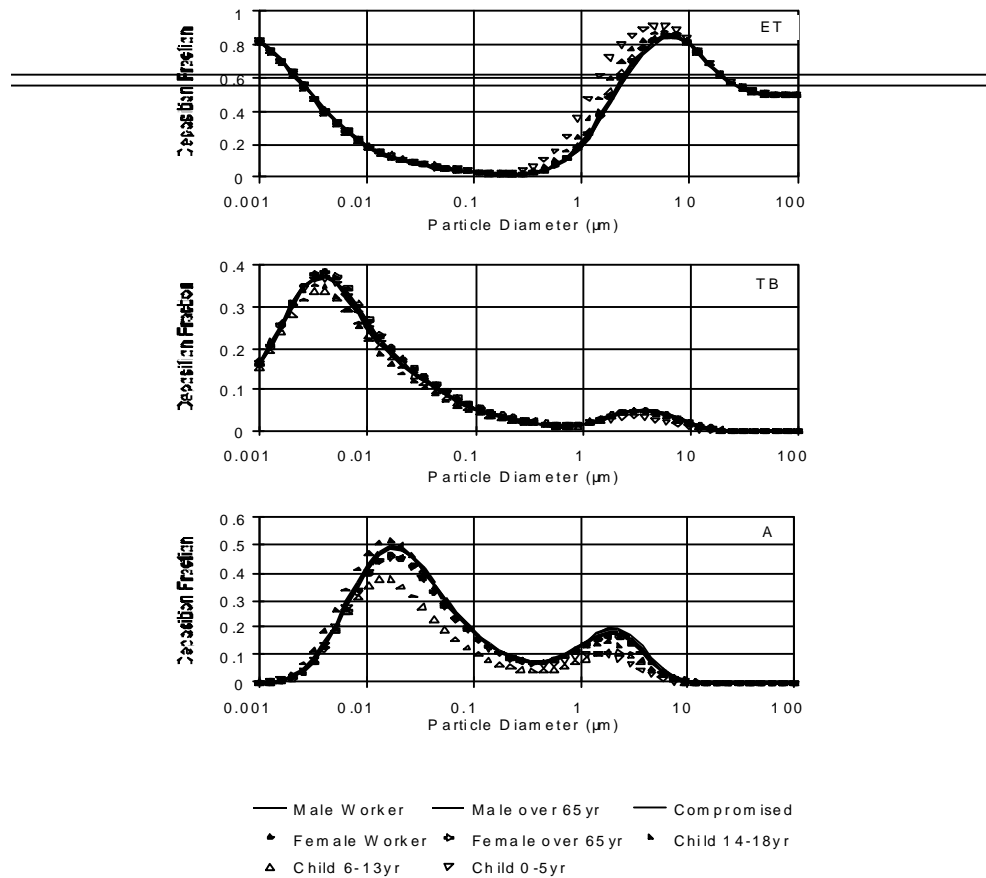
Figure 2. Daily mass particle deposition fraction in each respiratory tract region as predicted by the International Commission on Radiological Protection (ICRP66) (Source: U.S. EPA, 1995).

C.3. PM Doses in Children from Increased Ventilation Rates

While the fraction deposited on a mass basis is not generally very different between adults and children, differences in levels of activity between adults and children play a large role in age-related differences in their respective doses of ambient particles. Children generally have higher activity levels during the day (as noted above), yielding higher daily minute ventilation, especially when viewed on a per body weight basis. The typical total volume (m^3) breathed in 24 hours for children (0-5 years) is 11.6; children (6-13 years) is 18.2; and for children (14-18 years) is 25.5. The above childhood ventilation rates compare with an average 19.4 m^3 breathed in 24 hours for male worker (18-44 years of age). Thus, even without adjusting for body weight or lung surface area, teenagers breathe a greater volume of air than adults, due to their more active lifestyles, which increases the PM pollution dose they receive. Combining the deposition information in Figure 2 with these ventilation rates, it is seen in Figure

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3 that children generally receive a greater inhaled dose of particle mass per given ambient PM mass concentration, especially in children aged 14-18.
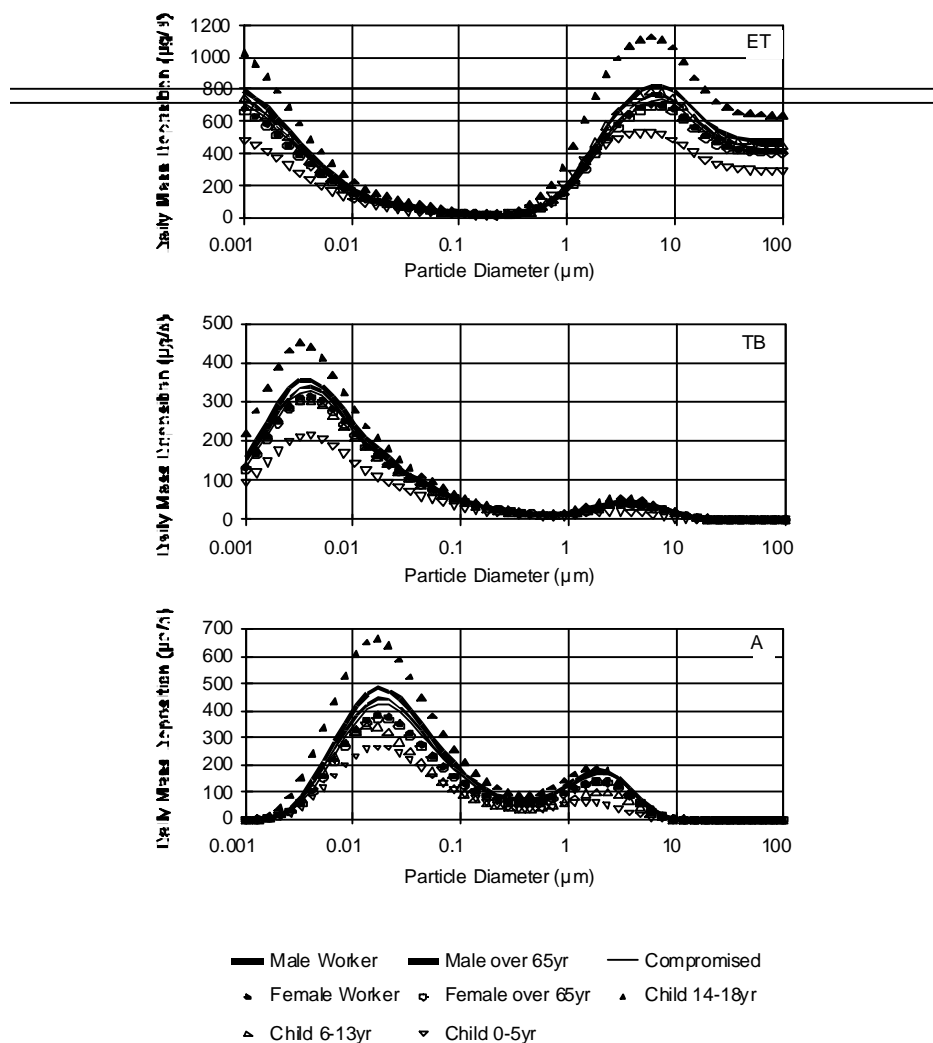

Figure 3. Daily PM deposition rates (ug/day) for 24 hour exposure at 50 ug/m^3 in each respiratory tract region as predicted by the International Commission on Radiological Protection (ICRP66).(U.S. EPA, 1996).

C.4. Doses of Ultrafines among Children 14-18 Years of Age

It is important to note, when evaluating the enhanced mass deposition in the ultrafine fraction for children 14-18 years of age, that the number of particle "hits" may be of paramount importance to health, rather than the PM_{10} mass. Thus, the enhanced alveolar deposition mass shown in Figure 3 in the ultrafine range represents a significant increase in the total number concentration dose experienced by children. The enormous numbers and huge surface area of the ultrafine particles demonstrate the importance of considering the size of the particle in assessing response. Ultrafine particles with a diameter of 20 nm when inhaled at the same mass concentration have a number concentration that is approximately 6 orders of magnitude higher

than for a 2.5 um diameter particle, and particle surface area is also greatly increased, as shown in Table 2.

Table 2.   Numbers and Surface Areas of Monodisperse Particles of Unit Density of Different Sizes at a Mass Concentration of 10 μg/m^3

Particle Diameter (μm)	Particle Number (per cm^3 Air)	Particle Surface Area (μm^2 per cm^3 Air)
0.02	2,400,000	3,016
0.1	19,100	600
0.5	153	120
1.0	19	60
2.5	1.2	24
Source: Oberdorster et al. (1995).		

If the number concentration exposure in the alveolar part of the lung is of great health significance, as has been hypothesized by Seaton et al. (1995), then the greater ultrafine exposure in children 14-18 could take on greater importance than the disparities indicated by adult versus childhood mass concentration exposures and doses.   Indeed, many studies summarized in the U.S. Environmental Protection Agency's PM Criteria Document (1995) suggest that the surface of particles, or substances that are on or are released from the surface (e.g., acids and/or transition metals), interact with the biological system and that surface-associated free radicals or free radical-generating systems may be responsible for toxicity. Thus, if ultrafine particles were to cause toxicity by a transition metal-mediated mechanism, for example, then the relatively large surface area for a given mass of ultrafine particles would mean higher concentrations of transition metals being available to cause oxidative stress to cells in the lungs of children vs. adults who breathe these aerosols.

C.5. Biological Factors that Increase PM Susceptibility in Children

In addition to differences in the ambient concentrations that children are exposed to relative to adults, the implications of those exposures are different due to biological differences between adults and children.   In this section, these differences and their implications are discussed.

C.5.1. Enhanced PM Doses in Children per Body Weight and Lung Surface

Area: In addition to the fact that children can get higher absolute PM doses due to their greater activities and higher PM personal clouds, children also have smaller lungs and much lower body weights, both of which increase the toxicity of a given PM dose. For example, a newborn typically weighs 3 kg, a young child 10 kg, an older child 33 kg, and an adult 70 kg (Snodgrass, 1992). Thus, PM doses, when viewed on a per kg body weight basis, are much higher for children than adults. This is graphically displayed in Figure 4, which indicates that the amount of air inhaled per kg body weight increases dramatically as age decreases below adult levels, with the inhalation rate (in m^3/kg/day) of a 10-year old being roughly twice that of a 30-year old person, and this estimate does not even consider the higher personal exposure concentrations that a child is usually exposed to as a result of his or her high activity levels. Thus, for a given exposure concentration, young children get roughly 3 times higher air pollution doses than do adults, when viewed on a per unit body weight basis.
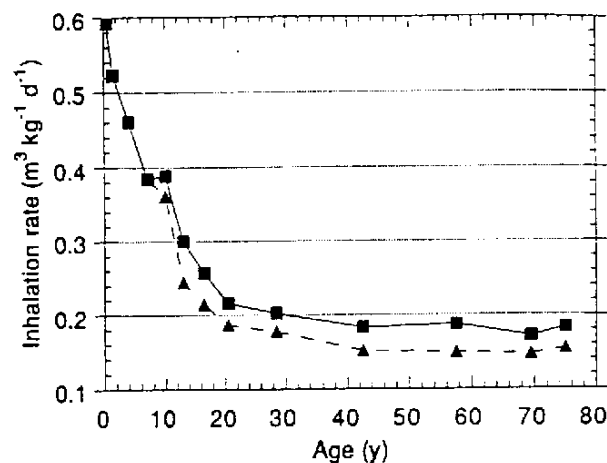

FIGURE 4. Age specific inhalation rates on a per body-weight basis for males (■) and females (▲).
(Adapted from Layton, 1993).

Child-adult dosage disparities are even greater when viewed on a per lung area basis, which may be more important than body weight if the number of particle "hits" per unit lung surface is the important health impact metric, which may well be the case for ultrafine particles. A newborn infant has approximately 10 million alveoli vs. some 300 million as an adult. The alveolar surface area increases from approximately 3 m^2 at birth to about 75 m^2 in adulthood,

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causing infants' and children's doses per lung surface area to be much higher than in adults, even given the same personal exposures (which is not the case, as they generally have greater PM_{10} personal exposures than adults, as noted above). Thus, PM air pollution doses are significantly higher in children than adults when one considers their higher personal exposures, their greater activity rates, and their smaller body weights and lung surface areas.

C.5.2. Diminished and Developing Defense Systems in Infants: As discussed by Plopper and Fanucchi (2000), the limited experimental and epidemiologic studies currently available identify the early post neonatal period of lung development as a time of high susceptibility for lung damage created by exposure to environmental toxicants. For example, due to the relatively diminished defenses of their developing immune systems, infants are disproportionately susceptible to infections and other diseases. Indeed, in 1998 in the U.S., the rate (per 1000) of Meningococcal disease by age group was 11.47 for <1 year versus: 2.75 for 1-4 years; 0.90 for 5-14 years; 1.27 for 15-24 years, 0.41 for 25-39 years; 0.49 for 40-64 years; and, 1.13 for >=65 years (CDC, 1999). Recent research indicates that there is a relationship between respiratory infections and air pollution effects in children (Sarafino et al., 1998). Thus, the higher rate of infectious diseases among infants is an indicator of diminished defenses against health insults, and is likely to cause them to have diminished reserves, and therefore to be more greatly affected by exposures to air pollution.

In addition to their insufficiently developed immune systems, infants are growing rapidly, and limited recent evidence supports the hypothesis that environmental pollution can significantly alter development of the respiratory system at that period of life. In experimental animals, for example, elevated neonatal susceptibility to lung-targeted toxicants has been reported at doses "well below the no-effects level for adults" (Plopper and Fanucchi, 2000; Fanucchi and Plopper, 1997). In addition, acute injury to the lung during early postnatal development causes a failure of normal repair processes, including down-regulation of cellular proliferation at sites of injury in animals. (Smiley-Jewel, et al., 2000, Fanucchi et al., 2000). Thus, it may be that both infants' diminished defenses and pollution-induced impairment of

repair mechanisms can therefore coincide during infancy, making the neonatal and post-neonatal period one of especially elevated susceptibility to damage by environmental toxicants like PM.

D. Key Studies of PM and Sulfate Health Effects

As discussed by Bates (1995), air pollution has been documented for many decades to be associated with a wide variety of health impacts in humans, and especially among the elderly and children. Indeed, as shown in the table below, infants less than one year of age (0-1 months Neonatal, 1-12 months Post-neonatal) experienced larger increases in mortality than older children or young adults during the notorious London Fog air pollution episode of 1952, and infants are indicated to be an especially susceptible subgroup of children. Among adults, recent research indicates that those with prior or coincident respiratory infections are among those especially affected by air pollution (Zanobetti et al, 2000), which may also be a factor placing infants at higher risk of being affected by air pollution, given their high rates of infectious diseases.

Table 3. Deaths Registered in London by Age Group (Adapted from Bates, 1995)							
	< 1 Month of Age	1-12 Mo. Old	1-14 Years of Age	15-44 Years of Age	45-64 Years of Age	65-74 Years of Age	75+ Years of Age
Week Before the Episode	16	12	10	61	237	254	335
Week After the Episode	28	26	13	99	652	717	949
Before/After Episode Ratio	1.75	2.17	1.3	1.62	2.75	2.82	2.83

More recent epidemiological evidence indicates that lower present-day ambient PM air pollution exposure is also associated with adverse health effects in children in general, and, as will be discussed in detail below, these effects can include:

From short-term PM exposures to children:

- reduced pulmonary function;

- increased respiratory symptoms in asthmatics (e.g., asthma attacks) and non-asthmatics;

- increased incidence of respiratory doctor's visits;

- increased incidence of emergency department (ED) visits and hospital admissions (HA's);

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- increased mortality, and;

- especially increased infant morbidity and mortality;

From long-term chronic PM exposures to children:

- Reduced lung function;

- increased respiratory symptoms; and,

- Increased infant mortality, intrauterine growth reduction, or pre-term delivery.

The PM indices most commonly evaluated in epidemiological and toxicological studies are those that have been most routinely measured: PM_{10}, total suspended particulate matter (TSP), and Black Smoke (BS, an index of primary carbonaceous particle mass collected primarily in Britain and Europe). However, significant effects are also reported for less often measured $PM_{2.5}$, sulfates ($SO_4^=$), and acidic aerosols (H^+).

This section seeks to summarize the most pertinent available evidence for acute and chronic health impacts of particulate matter and sulfates (including relevant toxicology, controlled exposures, and epidemiological studies, as available). These discussions emphasize studies involving children and adolescents, but rely on studies among adults when children's studies are not available. This section will also include, to the extent that information is available, a discussion of any special biological reasons for, or scientific evidence of, elevated susceptibility of infants and children to particulate matter and sulfates, in comparison to the general population.

D.1. Lung Function and/or Respiratory Symptom Effects from Acute PM Exposures

While not as adverse as more severe outcomes, such as medical visits or hospital admissions, symptom and lung function impacts do provide supportive evidence of consistent effects across outcomes, and can become medically important in health impaired individuals (e.g., children with asthma). A variety of PM and or sulfate symptom effects have been found in children, particularly in U.S. studies conducted in California. Cough, phlegm, and lower respiratory infections (LRI) are sometimes found to be associated with air pollution in these

studies. Delfino and colleagues' (1998) California study reported stronger symptom effects for 1-h and 8-h PM_{10} exposures, rather than 24-hr average PM_{10}, is noteworthy. This may indicate the need for a PM standard applicable to more acute exposure peaks of only a few hours.

Many asthmatics self-medicate with bronchodilators, which may also be a useful indicator of respiratory distress in these subjects. In the case of the Thurston et al. (1997) study of children with asthma at a summer camp, the medications were prescribed in cases where an asthma exacerbation was verified by a resident physician, indicating this to be a metric of severe air pollution effects associated with acidic sulfates (and ozone) in this case. A number of investigators have found statistically significant peak expiratory flow reduction (PEFR) associated with PM_{10} and other PM indices, and some have reported significant reduction in FEV_1 and FVC. For example, Figure 5 shows the relationship found between sulfates and PEFR, lower respiratory chest symptoms, and medication use in children with asthma in the Thurston et al summer camp study.
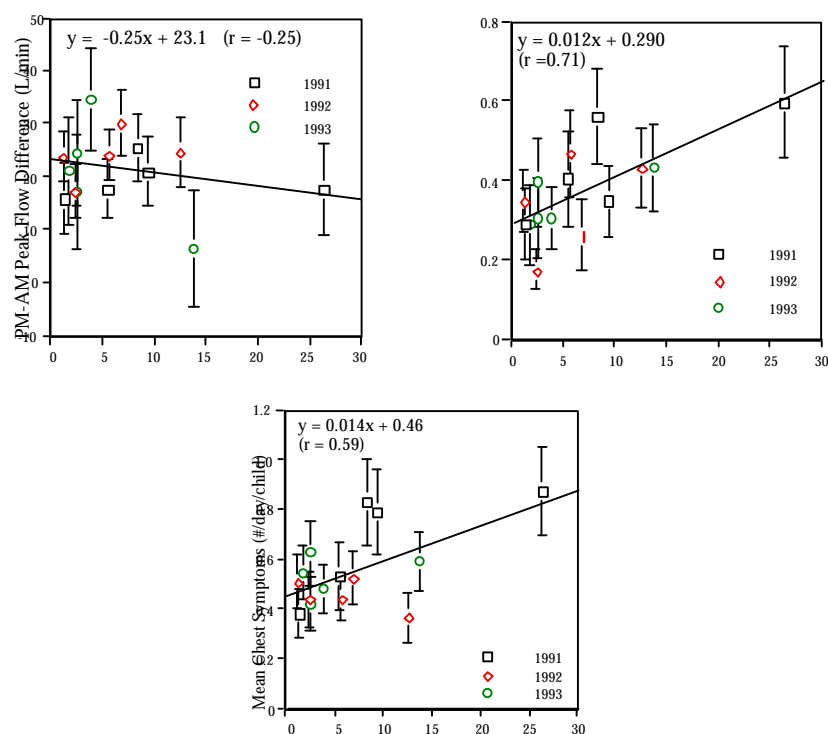

Figure 5. Lung Function, Symptom, and Inhaler Medication Use Association with Sulfate Concentration in Asthmatic Children (ages 8-12). (Adapted from Thurston et al., 1997).

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Thus, as indicated by the studies summarized in Table 4, there is an overall indication that respiratory symptoms in children are exacerbated by exposure to airborne particles and sulfates. These effects have greater health implications in children with asthma, and can and do lead to an increased incidence of asthma attacks. Since the prevalence of asthma is much higher among children than among adults (CDC, 1996a,b), these enhanced acute effects of air pollution on those with asthma put more children at higher risk of PM health effects than adults.

D.2. Lung Function and/or Respiratory Symptoms from Long-Term PM Exposures

For decades, there has been accumulating evidence suggesting that higher long-term ambient particulate matter exposures are associated with higher rates of chronic respiratory disease. Much of this evidence has been based on cross-sectional analyses, comparing disease or symptom prevalence rates in different communities with different average pollution levels (e.g., Ferris et al., 1973; 1976; Hodgkin et al., 1984; Mullahy and Portney, 1990). This type of study is able to indicate associations, but they are often criticized because these analyses cannot be controlled for confounding factors on an individual level, and are more likely to be subject to ecological confounding than prospective cohort studies. Also, chronic symptoms presumably occur as a result of long-term exposures, but cross-sectional analyses are not very informative as to whether, for example, it is the five-year average, the twenty-year average, or the number of times a given level is exceeded that is the relevant health effects exposure measure.

TABLE 4. Recent U.S. Panel Studies Of Pulmonary Function Tests or Acute Respiratory Symptoms Associated with PM Exposure in North American Children

Study	Health Endpoints	Ages (yrs.)	PM Effects	Pollutants Considered	Remarks (N)
Ostro et al. (1995) Los Angeles, CA	Asthma symptoms for at least six weeks	7-12	Shortness of breath risk, 9% per 10 ug/m^3 PM$_{10}$	PM$_{10}$, TSP, SO$_4$, NO$_3$, O$_3$, SO$_2$, NO$_2$	African-American (N = 83)
Delfino et al. (1998) Alpine, CA	Bothersome asthma symptoms	9-17	Symptoms signif. 1-h, 8-h PM$_{10}$, 24-h less signif.	PM$_{10}$, O$_3$ (others low)	Panel of asthmatics (N = 25)
Delfino et al. (1997) Alpine CA	Symptom score, bronchodilator use		PM$_{10}$ signif. dilator use	PM$_{10}$, O$_3$	Asthmatics (N = 13)
Delfino et al. (1996), San Diego, CA	Symptom scores, bronchodilator use		Signif. O$_3$ personal monitor, N.S. SAM O$_3$, PM$_{2.5}$	PM$_{2.5}$, O$_3$	Asthmatics (N = 12)
Hoek et al. (1998) re-analyses of 4 other studies in the U.S. and the Netherlands	PEF, large changes related to symptoms		Signif. PEFR, Cough PEFR N.S. PEFR N.S. PEFR N.S.	PM$_{10}$	Utah Valley Bennekom Uniontown St. College
Linn et al. (1996) southern CA	Pulmonary function		Morning FVC signif. PM5?, NO$_2$	PM5?, NO$_2$	School children (N = 269)
Thurston et al. (1997) Connecticut summer camp	lung function, symptoms, dilator use	8-12	SO$_4$, O$_3$ assoc. with symptoms, PEFR, dilator use	PM$_{10}$, SO$_4$, H+, O$_3$,	Asthmatic children (n=55)

Key: PEF = peak expiratory flow; PEFR = reduction in PEF; N.S.= not statistically significant (two-tailed, P > 0.05).

Source: Adapted from US EPA (1998)

More recently published articles have followed cohorts, answering the major criticisms of past studies by allowing confounder controls at the individual level. Abbey and colleagues (1991; 1993; 1995a,b) have reported results of a 10-year cohort study conducted at Loma Linda University in California with a large sample of nonsmoking adults. This follow-up allowed for measures of exposure over the 10-year period and for obtaining information on changes in chronic respiratory disease incidence over time. Abbey et al. (1995a) extends those earlier studies by analyzing associations between these chronic respiratory disease outcomes and both fine particles and sulfates. Logistic models were fitted using the mean concentration of these two pollutants, along with PM$_{10}$, ozone, and other pollutants. Fine particles were estimated from empirical estimates related to airport visibility. Regarding sulfates, a statistically significant association was observed with airway obstructive disease (AOD). Abbey and colleagues found no association with either SO$_2$ or NO$_x$, but sulfate exposure was associated with changes in the severity of AOD and chronic bronchitis over the ten-year study period.

Thus, new cases of disease were able to be analyzed in relation to pollution exposure for a matching time period in these studies, providing a more definitive concentration-response function for chronic respiratory disease, while confirming past "ecological" study results.

Children are likely to be at greater risk from long-term exposures because their bodies are growing, and their developmental processes, especially in the lung, may well be interfered with by air pollution exposures. Table 5 shows a number of recent studies involving school-age children indicating adverse respiratory effects from longer-term PM exposures. PM_{10} is not always significantly associated with adverse health effects in these studies, although other PM indicators sometimes are (e.g., $SO_4^=$, H^+). The mechanisms by which elevated PM exposure over long periods of time may be associated with increased risk of respiratory symptoms or decreased pulmonary function in children are not now understood, but may be analogous to the cumulative effects of smoking or environmental tobacco smoke (ETS) on the human respiratory system.

TABLE 5. Recent PM Studies Of Pulmonary Function Tests Or Respiratory Symptoms Associated With Long-Term PM Exposure In North American School-Age Children					
Study	**Endpoint**	**Ages (years)**	**Significant PM Associations**	**Pollutants Considered**	**Remarks (N)**
Dockery et al. (1996) 24 U.S. & Can.. Communities	Various	8-12	SO_4 signif. bronchitis; PM_{10} N.S. any endpoint	PM_{10}, PM2.1, SO_4, H+, SO_2, O_3	
Raizenne et al. (1996) 24 U.S., Canadian Communities	Pulmonary function	8-12	Strong signif. H+, Signif. PM_{10}	PM_{10}, PM2.1, SO_4, H+, SO_2, O_3	
Peters et al. (1999a,b) 12 So. CA communities	Asthma, bronchitis, cough, wheeze, lung function	9-12	PM_{10} signif. FVC, FEF25-75% N.S. FEV_1, symptoms, PEFR,		(N =150 each, in grades 4, 7)

Source: Adapted from US EPA (1998)

D.3. Incidence of Medical Visits and Hospital Admissions from Acute PM Exposures

Numerous studies have related acute PM exposure with an increased incidence of hospital admissions (e.g., see Figure 6), but only a limited number have specifically studied the subgroup that are children. Burnett et al (1994) examined the differences in air pollution-hospital admissions associations as a function of age in the province of Ontario. As shown in

Table 6, this analysis indicated that the largest percentage increase in admissions was found among infants (neonatal and post-neonatal, one year or less in age), just as was the case for the mortality effects during the London fog of 1952 (see Table 3).
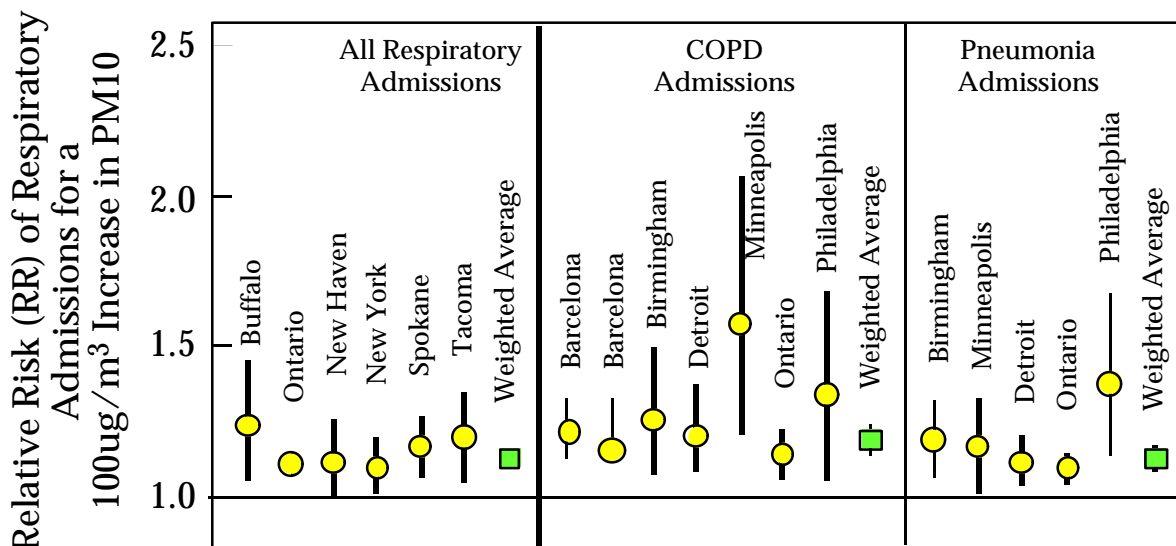

Figure 6. Relative Risk Estimates for Respiratory Hospital Admissions versus PM$_{10}$.
(Adapted from Schwartz, 1997)

Table 6. Age-Specific Percent Increase in Respiratory Hospital Admissions Associated with Sulfate (5.3 ug/m^3) and Ozone (50 ppb) in Ontario, Canada. (Adapted from Burnett et al, 1994)				
	< 1 Year of Age	2-34 Years of Age	35-64 Years of Age	75+ Years of Age
Asthma Admissions	13.0	5.5	9.8	7.0
Total Respiratory Admissions	14.8	5.5	7.2	4.3

More recent hospital admissions studies listed in Table 7 also indicate positive and often statistically significant associations between PM exposures and medical visits or hospital admissions by children. However, some of these PM-health effect associations listed in Table 7 became statistically non-significant when gaseous co-pollutants were included in the model, including O_3, SO_2, NO_2, CO. This may be due to a statistical artifact of pollutant inter-correlations over time causing enlarged coefficient standard errors, or may suggest that the co-pollutant mixture can collectively play a role in the effects of PM on children (e.g., through gas-particle interactions).

Looking in more detail at the results from each study in Table 7, as provided in Appendix A, reveals that the PM RR's for all children (e.g., 0-14 yrs.) are not usually noticeably larger than those for adults, but such comparisons of RR's must adjust for differences in the baseline risks for each group. For example, if hospital admissions per 100,000 per day for young children are double the rate for adults, then they will have a pollution relative risk (RR) per ug/m^3 that is half that of the adults given the exact same impact in admissions/100,000/ug/m^3/day. Thus, it is important to adjust RR's or Excess Risks (ER's) for each different age groups' baseline, but this information is usually not available (especially the population catchment for each age group in each study). One of the only signals that comes out clearly when comparing children with adults in Appendix A is for the group <1 yr. of age, which (despite higher baseline rates) usually has RR's larger than for other children or adults, as previously found in the Burnett (1994) study.

TABLE 7. Recent Key PM Studies Of Associations Between Medical Visits Or Hospital Admissions and Short-Term PM Exposure In Children

Study	Endpoint	Ages (yrs.)	PM Effects	Pollutants	Remarks (N)
Delfino et al. (1997) Montreal PQ	Emergency Dept. Visits (EDV), 1992-1993	0-1	H+ signif. only 1993	PM_{10}, $PM_{2.5}$, SO_4, H+, O_3	
Medina et al. (1997) Paris, France	Doctor's house calls	0-14	Asthma signif. BS.	PM_{13}, BS, SO_2, NO_2, O_3	Similar RR for PM13, SO_2, NO_2
Sunyer et al. (1997) Barcelona Helsinki London, Paris	emergency hospital admissions (HA's) for asthma	0-14	BS positive, N.S. NO_2 and SO_2 signif.	BS, NO_2, SO_2	
Anderson, et al. (1998) London, UK	HA's for asthma	0-14	BS positive, Signif.	BS, O_3, SO_2, NO_2	O_3, SO_2, NO_2, BS all pos. assoc.
Garty et al. (1998) Israel	EDV for asthma	1-18	PM_{10} N.S.	PM_{10}, O_3, SO_2, NO_2	N = 1076
Morgan et al, 1998 Sydney, AU	Asthma, COPD, and Cardiac HA's	0-14	PM (nephelometry) NS, NO_2 signif.	PM (nephelometry), O_3, and NO_2	
Rosas et al. (1998) Mexico City	emergency HA's for asthma	0-15	PM_{10} N.S.	PM_{10}, TSP, O_3, SO_2, NO_2	grass, fungal spores signif.
Atkinson et al. (1999) London UK	EDV for respiratory complaints	0-14	PM_{10} signif. total resp., asthma	PM_{10}, BS, O_3, SO_2, NO_2, CO	N.S. in 2-poll. models w. SO_2, NO_2
Atkinson et al. (1999) London UK	Hospital admissions for respiratory complaints	0-14	PM_{10} signif. total resp., asthma	PM_{10}, BS, O_3, SO_2, NO_2, CO	N.S. in 2-poll. models w. SO_2, NO_2
Norris et al. (1999) Seattle WA	EDV for asthma	0-17	PM_{10} signif. all hosp., lt.-scatter each	PM_{10}, light scatter, CO, SO_2, NO_2	PM_1 index from light scattering
Lin et al. (1999) Sao Paulo, Brazil	Respiratory emergency visits	0-12	PM_{10} signif. w. and w/o co-pollutants	PM_{10}, O_3, SO_2, NO_2, CO	LRI, URI, wheezing w. co-pollutants
Braga et al. (1999) São Paulo, Brazil	Hospital admissions	0-12	PM_{10} signif., not w. O_3, CO	PM_{10}, SO_2, NO_2, CO	
Ostro et al. (1999) Santiago, Chile	Medical visit for LRI, URI	<2 2-15	LRI 4-12% LRI 3-9%	PM_{10}, O_3	
Hajat et al. (1999) London U.K.	GP visits for asthma, LRI	0-14	PM_{10} N.S., BS signif. LRI	PM_{10}, BS, O_3, SO_2, NO_2, CO	
Wong, et al (1999) Hong Kong, CH	Respiratory HA's	0-4	PM_{10} NO_2, and O_3 signif., SO_2 not signif.	PM_{10}, NO_2, SO_2, O_3	
Gouveia et al (2000) Sao Paulo, BR	Respiratory, Pneumonia, and asthma HA's	<1 <5	Only PM signif., with larger RR than for <5 (pneumonia) All poll RR's>1, but NS. for asthma. Only SO_2 signif for Pneum., and only O_3 signif. for all resp.	PM_{10}, NO_2, SO_2, O_3	

Source: Adapted from US EPA (1998)

Two recent studies have found that air pollution-admissions associations are also stronger for the poor, which has special implications for children. Nauenberg et al. (1999) analyzed the effect of insurance status on the association between asthma-related hospital admissions and exposure to atmospheric particulate matter (PM_{10}) and ozone (O_3) using hospital discharge and air quality data for 1991-1994 for central Los Angeles. They used regression techniques with weighted moving averages (simulating distributed lag structures) to

measure the effects of exposure on overall hospital admissions, admissions of uninsured patients, admissions for which MediCal (California Medicaid) was the primary payer, and admissions for which the primary payer was another government or private health insurance program. No associations were found between asthma admissions and O_3 exposure in LA. An estimated increase from 1991 to 1994 of 50 micrograms per cubic meter in PM_{10} concentrations averaged over eight days was, however, associated with an increase of 21.0% in the number of asthma admissions. An even stronger increase--27.4%--was noted among MediCal asthma admissions. The authors conclude that low family income, as indicated by MediCal coverage, is a useful predictor of strength of asthma associations with air pollution. Similarly, Gwynn and Thurston (2000) have recently found that air pollution effects are worse in the poor and working poor than in other groups, and that these differences account for apparent racial differences in air pollution effects in New York City. These studies' results both indicate that children are especially at risk from air pollution, as they more often live in poverty than any other age group (e.g., in 1989, 27.3% of children in LA lived in poverty, as compared to 18.9% overall, and 10.5% for those 65+ years of age) (U.S. Census, 1994).

D.4. Infant and Child Mortality Associated with Acute PM Exposures

Table 8 shows the results of recent studies in which excess mortality was associated with PM. Significant mortality was reported in three of the four studies, using $PM_{2.5}$ exposure for infants in Mexico City (Loomis et al., 1999), TSP exposure for school- age children (but not younger children) in Delhi (Cropper et al., 1997), and PM_{10} exposure for a composite group of children 0-5 years in Bangkok (Ostro et al., 1998). Pereira et al. (1998) did not find excess stillbirths associated with PM_{10} in Sao Paulo. These studies are highly diverse in terms of age group, location, and environment. As with adult mortality, we do not now know the exact biological mechanisms that specifically account for excess child mortality from short exposures to PM at levels found in these Latin American and Asian countries. However, the available studies suggest that short-term PM exposure in general may cause deaths of some children in urban environments. The mortality findings are consistent with findings noted above of less

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serious health effects from short-term PM exposure, including lung function decreases, respiratory symptoms, asthma attacks and medical visits that may affect substantial numbers of children.

Table 8. Neonatal, Infant, And Child Mortality Attributable To Short-Term PM Exposure					
Study	Mortality	Ages	PM Effects	Pollutants	Remarks (N)
Loomis et al. (1999) Mexico City	Total	0-11 mo.	$PM_{2.5}$ signif. w and w/o co-pollutant	$PM_{2.5}$, O_3, NO_2	
Pereira et al. (1998) Säo Paulo, Brazil	Intrauterine	0 d	PM_{10} N.S.	PM_{10}, O_3, SO_2, NO_2, CO	
Cropper et al. (1997) Delhi, India	Total, cardiovascular, respiratory	0-4 yr. 5-14 yr.	TSP N.S. for total mort. TSP signif. for total mort	TSP, SO_2, NO_x	Similar RR in both age groups
Ostro et al. (1999) Bangkok, Thailand	Total, cardiovascular, respiratory	0-5 yr.	PM_{10} signif. all	PM_{10}, $PM_{2.5}$	

Source: Adapted from US EPA (1998)

D.5. Increased Infant and Child Mortality Associated with Long-Term PM Exposures

A number of studies suggest that the very young represent an especially susceptible sub-population, although the precise magnitude of the effects of specific levels of air pollution can be expected to vary with other underlying conditions. Lave and Seskin (1977) found mortality among those 0-14 years of age to be significantly associated with TSP. More recently, Bobak and Leon (1992) studied neonatal (ages less than one month) and post-neonatal mortality (ages 1-12 months) in the Czech Republic, finding significant and robust associations between post-neonatal mortality and PM_{10}, even after considering other pollutants. Post-neonatal respiratory mortality showed highly significant associations for all pollutants considered, but only PM_{10} remained significant in simultaneous regressions. Woodruff et al. (1997) used cross-sectional methods to follow-up on the reported post-neonatal mortality association with outdoor PM_{10} pollution in a U.S. population. This study involved an analysis of a cohort consisting of approximately 4 million infants born between 1989 and 1991 in 86 U.S. metropolitan statistical areas (MSA's). After adjustment for other covariates, the odds ratio (OR)

and 95% confidence intervals for total post-neonatal mortality for the high exposure versus the low exposure group was 1.10 (CI=1.04-1.16). In normal birth weight infants, high PM_{10} exposure was associated with mortality for respiratory causes (OR = 1.40, CI=1.05-1.85) and also with sudden infant death syndrome (OR = 1.26, CI=1.14-1.39). Among low birth weight babies, which are lower in counts (and therefore with greater uncertainty and power) high PM_{10} exposure was associated, but not significantly, with mortality from respiratory causes (OR = 1.18, CI=0.86-1.61).

The Woodruff et al. (1997) study was recently corroborated by a more elegant follow-up study by Bobak and Leon (1999), who conducted a matched population-based case-control study covering all births registered in the Czech Republic from 1989 to 1991 that were linked to death records. They used conditional logistic regression to estimate the effects of suspended particles, sulfur dioxide, and nitrogen oxides on risk of death in the neonatal and post-neonatal period, controlling for maternal socioeconomic status and birth weight, birth length, and gestational age. The effects of all pollutants were strongest in the post-neonatal period and were specific for respiratory causes. Only particulate matter showed a consistent association when all pollutants were entered in one model. Thus, it appears that PM is the air pollutant metric most strongly associated with excess post-neonatal deaths.

Collectively, all the recent studies of children less than one year old presented in Table 9 indicate severe adverse consequences to the mother, fetus, and infant from prolonged PM exposure during and shortly after pregnancy. There appears to be a possible relationship between preterm birth (< 37 weeks gestational age) or low birth weight (< 2,500 g) and PM exposure in several locations. A significant relationship with PM_{10} and $PM_{2.5}$ was found in Teplice, Czech Republic (Dejmek et al., 1999), but not with PM_{10} in Los Angeles (Ritz and Yu, 1999). In the case of Ritz and Yu, CO was significant, which might well be serving as an index of traffic-related pollution effects, and therefore possibly related to diesel particulate matter (DPM), but this is not evaluated. Bobak and Leon (1999) did not find a relationship of low birth weight to TSP. There was a significant risk of low birth weight and pre-term delivery in Beijing

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(Xu et al., 1995; Wang et al., 1997) associated with TSP, but SO_2 was the only co-pollutant considered. However, low birth weight is known to be an important risk factor for infant mortality, so that the findings of excess mortality in U.S. and Czech infants (Woodruff et al., 1997; Bobak and Leon, 1999) are consistent with many of the other findings on intrauterine growth reduction (IUGR), which is supportive of a causal relationship between PM exposure and adverse health effects in this age group.

Several methodological differences across studies make generalized conclusions more difficult to make. Dejmek et al. (1999) characterize IUGR as low-weight-for-gestational-age, whereas others use a fixed weight for full-term infants (37 to 44 weeks) without adjusting for gestational age. Dejmek et al. (1999) also find the average PM during the first month of pregnancy as the index of fetal exposure, whereas Xu et al. (1995), Wang et al. (1997), and Ritz and Yu (1999) use final trimester averages. Despite these methodological differences, there appears to be an identifiable PM risk to the fetus and infant.

A very recent study of infant mortality in U.S. counties indicates that these effects can occur in the U.S., as well (Chay and Greenstone, 1999). This study uses sharp, differential air quality changes across sites attributable to geographic variation in the effects of the 1981-82 recession to estimate the relationship between infant mortality and particulate matter air pollution. It is shown that, in the narrow period of 1980-82, there was substantial variation across counties in changes in particulate (TSP) pollution, and that these differential pollution reductions appear to be independent of changes in a multitude of other socio-economic and health care factors that may be related to infant mortality. The authors find that a 1 ug/m^3 reduction in TSP resulted in about 4-8 fewer infant deaths per 100,000 live births at the county level of the roughly 1,300 U.S. infant deaths in the first year of life per 100,000 live births (a 0.35-0.45 elasticity). The estimates are remarkably stable across a variety of specifications. The estimated effects are driven almost entirely by fewer deaths occurring within one month and one day of birth (i.e., neonatal), suggesting that fetal exposure to pollution may have adverse health consequences. The estimated effects of the pollution reductions on infant birth weight in

this study provide evidence consistent with the infant mortality effects found, suggesting a causal relationship between PM exposure and infant mortality, especially in the first month of life.

Table 9. Adverse Infant Health Effects Associated With Long-Term PM Exposure					
Study	Effects	Ages	PM Effects	Pollutants	Remarks (N)
Bobak and Leon (1992) Czech. Repub.	Total infant mortality, respir. mort.	0+ d neonatal post-neonatal post, respir.	TSP-10 N.S. TSP signif. TSP signif.	TSP-10, SO_2, NO_x	Ecologic study; TSP indexed as 90th percentile
Bobak and Leon (1999) Czech. Rep.	Low birth wt. Stillbirth	0 d	TSP N.S.	TSP, SO_2, NO_x	
Chay and Greenstone (1999) California Counties	Infant mortality	0-1 yr.	TSP Signif.	TSP	1 ug/m^3 reduction associated with 4-8 fewer deaths per 100k live births
Dejmek et al. (1999) Teplice, Czech. Rep.	Intrauterine growth reduction	0 d	First month $PM_{2.5}$ > 37, PM_{10} > 40 signif.	PM_{10}, $PM_{2.5}$, SO_2, NO_x, PAH	30-d avg. PM per month of pregnancy
Ritz and Yu (1999) Los Angeles, CA	Low birth weight (adj. Gest age)	0 d	Last trimester PM_{10} N.S.	PM_{10}, O_3, NO_2, CO	CO signif., may be index of traffic air poll., e.g. DPM
Wang et al. (1997) Beijing, PRC	Low birth weight	0 d.	TSP signif. increases risk of LBW	TSP, SO_2 in third trimester	SO_2 also signif. Small reduc. mn.wt.
Woodruff et al. (1997)	Total infant mortality, SIDS, resp.	1-11 mo.	PM_{10} signif. total, SIDS, respir. NBW	PM_{10}	PM_{10} avg. over 2 mos.
Xu et al. (1995) Beijing, PRC	Preterm gestational age	0 d	TSP signif. lag 5-10 days	TSP, SO_2	SO_2 also signif.

Source: Adapted from US EPA (1998)

D.6. Evidence for a Role of Sulfates in PM Health Effects

The characteristics of particles responsible for the adverse health effect associations of PM are not yet known. However, lung injury has been postulated to be mediated by ultrafine particles, biological agents (e.g., endotoxin), acid aerosols, organic fraction of PM and oxidant generation catalyzed by transition metals associated with particles. Of these, the role of acidic combustion aerosols and their possible mechanisms for effects are among the best documented.

While significant associations are sometimes reported between total suspended particulate (TSP) and health effects in large populations, the degree of association in studies comparing various PM indices (e.g., Ozkaynak and Thurston, 1987; Dockery et al., 1993; Thurston et al., 1994) is as follows:

$$TSP < PM_{10} < PM_{2.5} < SO_4^=$$

Each metric is essentially a subset of the one to its left, implying that $SO_4^=$, or something in the mixture closely associated with it, is a likely causal factor in the effects reported.

The sulfate ion itself is an unlikely causal factor if it is in a neutralized state. It is already present in body fluids at relatively high concentrations, and controlled inhalation studies in humans and laboratory animals of pH neutral or nearly neutral sulfate salts, such as ammonium sulfate $[(NH_4)_2SO_4]$, even at relatively high concentrations, produce none of the effects reported from the epidemiologic studies (Utell et al., 1983; Lippmann et al., 1987; Schlesinger, 1989; Schlesinger et al., 1990). What these controlled exposure studies do show is that sulfate aerosols containing strong acids, such as sulfuric acid (H_2SO_4) and, to a lesser extent, ammonium bisulfate (NH_4HSO_4), do produce functional and structural changes in healthy subjects consistent with those observed in epidemiological studies, and do so at exposures within the upper bounds of current H^+ ambient levels. Furthermore, it is reasonable to speculate that the effects seen in the epidemiological studies are occurring in hyper-susceptible segments of the population, and that controlled exposure studies in susceptible human and animal cohorts, if they could be ethically performed, might well produce comparable effects at low ambient levels of H^+. A working hypothesis, therefore, is that H^+ is a causal factor for human health effects (e.g., see Lippmann and Thurston, 1996) and that, among the commonly measured PM indices, $SO_4^=$ is the best surrogate metric for H^+.

Historical and present-day evidence suggest that there can be both acute and chronic effects by acidic sulfates on human health. Evidence from historical pollution for episodes, notably the London Fog episodes of the 1950's and early 1960's, indicate that extremely elevated daily acid aerosol concentrations (on the order of 400 ug/m^3 as H_2SO_4, or roughly 8,000 nmoles/m^3 H^+) may be associated with excess acute human mortality when present as a co-pollutant with elevated concentrations of PM and SO_2 (Ministry of Health of Great Britain, 1954). In addition, Thurston et al. (1989) and Ito et al. (1993) both found significant

associations between acid aerosols and mortality in London during non-episode pollution levels (30 ug/m^3 as H_2SO_4, or approximately 600 nmoles/m^3 H$^+$), though these associations could not be separated from those for BS or SO_2.

Attempts to date to associate present-day levels of acidic aerosols in the U.S. with acute and chronic mortality (Dockery et al., 1992; Dockery et al., 1993, Schwartz et al., 1996, and Gwynn, et al., 2000) have had more mixed results, but there may not have been a sufficiently long series of H$^+$ measurements to detect H$^+$ associations in many of these studies. In the Utah Valley studies (Pope et al. 1991, 1992), PM_{10}-health effects association were found, despite limited H$^+$ sampling indicating low acid aerosol levels. This is not inconsistent with adverse health effects from H$^+$, however, when it is considered that PM can contain numerous toxic agents other than H$^+$. The more recent work of Gwynn et al. (2000) reported significant pollutant-health effect associations in Buffalo, NY--most strongly between $SO_4^=$ and respiratory hospital admissions (as indicated by its t-statistic). Additionally, H$^+$ and $SO_4^=$ demonstrated the most coherent associations with both respiratory hospital admissions and respiratory mortality. The authors concluded that "acidic sulfate aerosols represent a component of PM air pollution that may contribute to the previously noted adverse effects of PM mass on human health."

Pope et al. (1995) linked ambient air pollution data from 151 U.S. metropolitan areas in 1980 with individual risk factor on 552,138 adults who resided in these areas when enrolled in a prospective study in 1982. Deaths were ascertained through December 1989. Exposure to $SO_4^=$ and $PM_{2.5}$ pollution was estimated from national databases. The relationships of air pollution to all-cause, lung cancer, and cardiopulmonary mortality were examined using multivariate analysis that controlled for smoking, education, and other risk factors at the individual level. An association between mortality and particulate air pollution was observed. Figure 7 shows the range of values for the adjusted mortality rates in the various communities versus annual average $SO_4^=$ concentrations. The Pope et al. (1995) results thus indicate that the concerns raised about the credibility of the earlier results, due to their inability to control for potentially confounding factors such as smoking and socioeconomic variables on an individual

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level, can be eased, and these findings are consistent with the prior findings of Ozkaynak and Thurston (1987) and Lave and Seskin (1970, 1977). Adjusted relative risk ratios (and 95% confidence intervals) of all-cause mortality for the most polluted areas compared with the least polluted were $RR(SO_4^=)$ =1.15 (1.09 to 1.22) and $RR(PM_{2.5})$ = 1.17 (1.09 to 1.26). The findings of Dockery et al. (1993) and Pope et al. (1995) in prospective cohort studies also indicate that mean lifespan shortening of long-term exposures to PM is of the order of two years (Brunekreef, 1997). This implies that some individuals in the population have lives shortened by many years, and that there is excess mortality associated with long-term fine particle exposure that is greater than that indicated by an accumulation of acute effect estimates provided by the time-series studies of daily mortality.
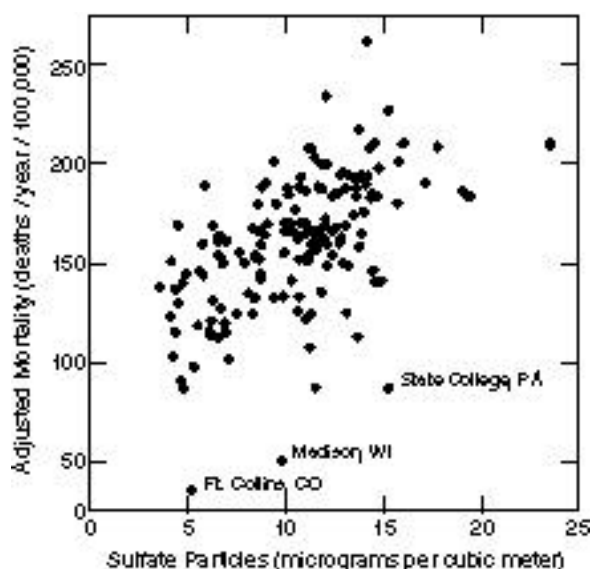

Figure 7. **Age-, sex-, and race-adjusted population-based mortality rates versus mean sulfate air pollution levels for 1980.** (Adapted from Pope, C.A. et al., Am. J. Respir. Crit. Care Med. 151:669-674 (1995).

Increased hospital admissions for respiratory causes were also documented during the London Fog episode of 1952, and this association has also been observed under present-day conditions. Thurston et al. (1992) and Thurston et al. (1994) have noted associations between ambient acidic aerosols and summertime respiratory hospital admissions in both New York State and Toronto, Canada, respectively, even after controlling for potentially confounding

temperature effects. In the latter of these studies, significant independent H^+ effects remained even after simultaneously considering the other major co-pollutant, O_3, in the regression model. While the New York State study considered only ozone as a possible confounder, the Toronto study also considered NO_2 and SO_2, but found them to be non-significant. In the Toronto analysis, the increase in respiratory hospital admissions associated with H^+ was indicated to be roughly six times that for non-acidic PM_{10} (per unit mass). In these studies, H^+ effects were estimated to be the largest during acid aerosol episodes ($H^+ > 10$ ug/m^3 as H_2SO_4, or 200 nmoles/m^3 H^+). These studies provide evidence that present-day strongly acidic aerosols can represent a portion of PM which is particularly associated with significant acute respiratory disease health effects in the general public.

Burnett et al. (1994) has related the number of emergency or urgent daily respiratory admissions at 168 acute care hospitals in all of Ontario during 1983 to 1988 to estimates of ozone and sulfates in the vicinity of each hospital. The authors reported that SO_2 and NO_2 were only weakly correlated with SO_4 in these data ($r = 0.3$), so these pollutants were unlikely to be confounders. Long-wave cycles in the admissions data were removed using a 19-day moving average equivalent high pass filter. A random effects model (wherein hospital effects were assumed to be random) was employed, using the generalized estimating equations (GEE). After adjusting admissions data for seasonal patterns, day of week effects, and individual hospital effects, positive and statistically significant associations were found between hospital admissions and both ozone and sulfates lagged 0 to 3 days. Positive associations were found in all age groups (0 to 1, 2 to 34, 35 to 64, 65+). The bivariate relationship found between adjusted admissions and sulfates in these data are shown in Figure 8. Positive and significant air pollution associations were found for asthma, chronic obstructive pulmonary disease (COPD), and infections, but not for nonrespiratory (control) admissions, nor for respiratory admissions in the winter months (when people are indoors and levels of these pollutants are low). While these analyses employed much more sophisticated statistical methods, the results generally consistent with Bates and Sizto's prior work in this region, though ozone was found to

yield a larger effect than sulfates in this study. The authors point out that $PM_{2.5}$ and H^+ are highly intercorrelated with sulfates in the summer months ($r > 0.8$), and that one of these agents may be responsible for the health effects relationships found with sulfates in this work.

Ostro (1988) also conducted a cross-sectional analysis of the U.S. Inhalable Particle Monitoring Network airborne particulate matter dataset, but analyzed the 1979-1981 annual Health Interview Surveys (HIS) to test if there were morbidity associations coherent with those found for mortality by Ozkaynak and Thurston during this period. Ostro reported a stronger association between several measures of morbidity (work loss days, restricted activity days, etc.) and lagged fine particle estimates than found with prior 2-week average TSP levels in 84 U.S. cities. In this analysis, a Poisson model was employed, due to the large number of days with zero cases in the dependent variables, and the analyses focused on adults aged 18 to 65. Smoking was not considered in the model, since not all metropolitan areas had data, but the correlation between smoking and any of the pollutants was less than 0.03 and non-significant in the one-third of the HIS sample for which smoking data were available. This indicates that, while presumably important to morbidity, smoking is not a confounder to pollutants in such cross-sectional analyses. Ostro concluded that his findings were consistent with the results of prior cross-sectional analyses reporting an association between mortality and exposures to fine particles and sulfates.
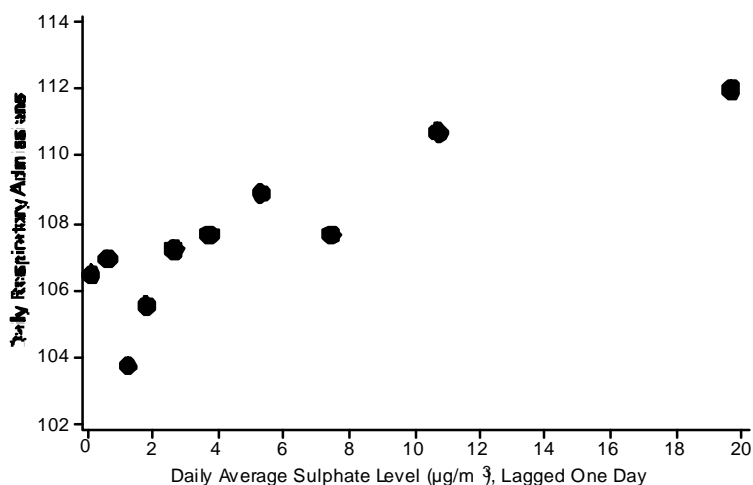

Figure 8. Average number of respiratory admissions Ontario hospitals by decile of the daily average sulfate level (ug/m^3), 1 day lag. (Adapted from Burnett et al., 1994).

Taken as a whole, these analyses are suggestive of mortality and morbidity associations with the sulfate fraction of fine particles found in contemporary American urban airsheds. Without nationwide measurements of airborne acidity, however, it is not now possible to evaluate the relative contribution of acid aerosols within these fine particle sulfates to the reported health effects.

Results from recent acute symptoms and lung function studies of healthy children indicate the potential for acute acidic sulfate effects in this population. While the 6-City study of diaries kept by parents of children's respiratory and other illness did not demonstrate H^+ associations with lower respiratory symptoms, except at H^+ above 110 moles/m$_3$ (Schwartz et al., 1994), upper respiratory symptoms in two of the cities were found to be most strongly associated with daily measurements of H_2SO_4 (Schwartz, et al., 1991b). Some, but not all, recent summer camp and school children studies of lung function have also indicated significant associations between acute exposures to acidic PM and decreases in the lung function of children independent of those associated with O_3 (Studnicka et al., 1995; Neas et al., 1995).

Studies of the effects of chronic H^+ exposures on children's respiratory health and lung function are generally consistent with effects as a result of long-term H^+ exposure. Preliminary analyses of bronchitis prevalence rates as reported across the 6-City study locales were found to be more closely associated with average H^+ concentrations than with PM in general (Speizer, 1989). A follow-up analysis of these cities and a seventh locality which controlled the analysis for maternal smoking and education and for race, suggested associations between summertime average H^+ and chronic bronchitic and related symptoms (Damokosh et al., 1993). The relative odds of bronchitic symptoms with the highest acid concentration (58 nmoles/m^3 H^+) versus the lowest concentration (16 nmoles/m^3) was 2.4 (95% CI: 1.9 to 3.2). Furthermore, in a follow-up study of children in 24 U.S. and Canadian communities (Dockery et al., 1996) in which the analysis was adjusted for the effects of gender, age, parental asthma, parental education, and parental allergies, bronchitic symptoms were confirmed to be significantly associated with

strongly acidic PM (relative odds = 1.66, 95% CI: 1.11 to 2.48). It was also found that mean

FVC and $FEV_{1.0}$ were lower in locales having high particle strong acidity (Raizenne et al., 1996).

Thus, epidemiological evidence indicates that chronic exposures to strongly acidic PM can have

effects on measures of respiratory health in children.

One plausible mechanism by which acidic sulfates may act to increase the toxicity of PM

is by enhancing the effects of soluble metals and reactive oxygen intermediates. PM, and

especially combustion-related aerosols, contain transition metals such as iron, copper, nickel,

vanadium, and cobalt that are more readily soublized at lower pH. These metals are capable of

catalyzing the one-electron reductions of molecular oxygen necessary to generate reactive

oxygen species (ROS) (e.g., via the iron-catalyzed Fenton Reactions. Other than Fe, several

vanadium compounds have been shown to increase mRNA levels for selected cytokines in BAL

cells and also to induce pulmonary inflammation (Pierce et al., 1996). $NaVO_3$ and $VOSO_4$,

highly soluble forms of vanadium, tended to induce pulmonary inflammation and inflammatory

cytokine mRNA expression more rapidly and more intensely than the less soluble form, V_2O_5, in

rats. Neutrophil influx was greatest following exposure to $VOSO_4$ and lowest following exposure

to V_2O_5, providing one plausible sulfate PM health effects mechanism.

Many studies investigating the response of animals to particle exposures have used

residual oil flyash (ROFA) as a surrogate for ambient particles. ROFA has a high content of

water soluble sulfate and metals. As described in the last U.S. PM Criteria Document (U.S.

Environmental Protection Agency, 1995), intratracheal instillation of high doses of ROFA

suspension generally produced severe inflammation, an indicator of pulmonary injury that

included recruitment of neutrophils, eosinophils, and monocytes into the airway. The biological

effects of ROFA have been shown to depend on aqueous leachable chemical constituents of

the particles. Dreher et al. (1997) have shown that a leachate prepared from ROFA, containing

predominantly Fe, Ni, V, Ca, Mg, and sulfate, produced similar lung injury to that induced by the

complete ROFA suspension, indicating the potency of this sulfate-metals mixture.

E. PM and Sulfate Interactions with Other Pollutants

This section addresses any studies examining interactions between PM and sulfates and other pollutants (including noncriteria pollutants or bioaerosols).

E.1. Interaction of PM with Allergens

There is growing scientific evidence that particulate matter from fossil fuel combustion enhances the immune response to allergens, leading to an increase in allergic inflammation and allergic reactivity. Therefore, particulate air pollutants can be an important contributor to the increased morbidity of acute asthma and allergic rhinitis, as well as being a potential trigger of asthma in its own right. Furthermore, recent clinical studies and experimental studies have been able to describe the manner in which diesel particles specifically trigger a biochemical reaction which causes the type of allergic inflammation that asthma medications are aimed at preventing (e.g., see: Nel et al., 1998). Nel and colleagues (1998) have suggested that the rise in the U.S. prevalence rate for allergic rhinitis (5% in the 1950s to about 20% in the 1980s) may be related to increased diesel particulate matter (DPM), in addition to other combustion related PM. Combustion particles may also serve as carrier particles for allergens (Knox et al., 1997). These studies provide biological plausibility for the exacerbation of allergic asthma associated with episodic exposure to PM. Although DPM may make up only a fraction of the mass of urban PM, because of their small size, DPM may represent a significant fraction of the ultrafine particle mode in urban air, especially in cities that rely heavily on diesel-powered vehicles. Thus, while not themselves allergens, diesel and other combustion PM may increase an asthma patient's general responsiveness to any and all allergens and pollens to which they are already allergic, thereby increasing the chance that acute asthma problems will be experienced in a given population of persons with asthma.

Alterations in the response to a specific antigenic challenge have also been observed in animal models at high concentrations of acid sulfate aerosols (above 1,000 ug/m^3) (Pinto et al., 1979; Kitabatake et al., 1979; Fujimaki et al., 1992). Several studies have reported an enhanced response to non-specific bronchoprovocation agents, such as acetylcholine and

histamine, after exposure to inhaled particles. This non-specific airway hyperresponsiveness, a central feature of asthma, occurs in animals and human subjects exposed to sulfuric acid under controlled conditions (Gearhart and Schlesinger, 1986; Utell et al., 1983). Although its relevance to specific allergic responses in the airways of atopic individuals is unclear, it demonstrates that the airways of asthmatics may become sensitized by acidic sulfates to either specific or non-specific triggers that could result in increases in asthma severity and asthma-related hospital admissions (Peters et al., 1997; Lipsett et al., 1997).

The above noted PM-asthma interactions are of greatest significance to children because the prevalence of asthma children is higher and increasing more rapidly among children than among other age groups. Indeed, the U.S. prevalence rate of asthma in children aged <20 years rose rapidly from approximately 3.5% to 5% during the 1980's, a prevalence that was nearly double adults 20-64 years of age at that time, and higher than all other age groups (U.S. DOH, 1991). Rates for asthma prevalence, hospitalization, and death are especially high among children residing in inner cities, and important risk factors for asthma-related mortality include being poor or black (CDC, 1997a, 1997b). Thus, the above discussed PM-asthma interactions, that suggest that PM air pollution exposure makes people with asthma more reactive to all asthma triggers, mean that children will be at greater risk from PM exposure, as they have the highest prevalence and severity of this worsening disease.

E.2. Interaction of PM with Gaseous Pollutant Mixtures

Ambient PM usually co-exists in indoor and outdoor air with a number of co-pollutant gases, including ozone, sulfur dioxide, oxides of nitrogen, and carbon monoxide, and this may modify PM toxicity. The presence and nature of any interactions are not well understood at this time, but are likely to depend upon the particle size and the concentration of pollutants in the mixture, exposure duration, and the health endpoint being examined.

One of the primary particle-gas interaction mechanisms documented to-date are chemical interactions between particles and gases that occur on particle surfaces. This forms secondary products on that particle surface that may be more toxicologically active than the

primary materials, and that can then be more readily carried to a sensitive sites deeper in the lung. The hypothesis of such chemical interactions has been evaluated in the gas and particle exposure studies of SO_2 and particles by Amdur and colleagues (Amdur and Chen, 1989; Chen et al., 1992). These investigators have demonstrated that synergism occurs as secondary chemical species are produced (e.g., sulfuric acid on the surface of the particles), especially under conditions of elevated relative humidity, such as found in the human lung. Thus, these studies suggest that air quality standards set for individual air pollutants may not be fully protective of human health for exposures to mixed ambient pollutants.

Another hypothesized mechanism of gas-particle interaction may involve pollutant-induced changes in the lung, enhancing the effects of the co-pollutant. For example, Last et al. (1984) indicated that the observed synergism between ozone and acid sulfates in rats was due to a decrease in the local microenvironmental pH of the lung following deposition of acid, enhancing the effects of ozone by producing a change in the reactivity or residence time of reactants, such as radicals, involved in ozone-induced tissue injury. Kleinman et al. (1999) examined the effects of ozone plus fine H_2SO_4 coated carbon particles (MMAD = 0.26 um) for 1 or 5 days. They found the inflammatory response with the ozone-particle mixture was greater after 5 days (4 hours/day) than after day 1. This contrasted with ozone exposure alone (0.4 ppm) which caused marked inflammation on acute exposure, but no inflammation after 5 consecutive days of exposure. Thus, acids and ozone together appear to be of greater impact than either alone.

Two studies have examined interaction between carbon particles and gaseous co-pollutants. Jakab et al. (1996) challenged mice with a single 4-hour exposure to a high concentration of carbon, 10 mg/m^3, in the presence of SO_2 at low and high relative humidity. Macrophage phagocytosis was significantly depressed only in mice exposed to the combined pollutants under high relative humidity conditions. This study demonstrates that fine carbon particles can serve as an effective carrier for acidic sulfates, where chemical conversion of adsorbed SO_2 to acid sulfate species occurred. Interestingly, the depression in macrophage

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function was present as late as 7 days post-exposure. Bolarin et al. (1997) exposed rats to only 50 or 100 ug/m^3 carbon particles in combination with ammonium bisulfate and ozone. Despite 4 weeks of exposure, they observed no changes in protein concentration in lavage fluid or blood prolyl 4-hydroxylase, an enzyme involved in collagen metabolism. Slight decreases in plasma fibronectin were present in animals exposed to the combined pollutants versus ozone alone. Thus, the potential for adverse effects in the lungs of animals challenged with a combined exposure to particles and gaseous pollutants is dependent on numerous factors including the gaseous co-pollutant, concentration, and time.

Linn and colleagues (1997) examined the effect of a single exposure to 60 to 140 ug/m^3 H_2SO_4, 0.1 ppm SO_2, and 0.1 ppm ozone in healthy and asthmatic children. The children performed intermittent exercise during the 4-hour exposure to increase the inhaled dose of the pollutants. An overall effect on the combined group of healthy and asthmatic children was not observed. A positive association between acid concentration and symptoms was seen, however, in the subgroup of asthmatic children. The combined pollutant exposure had no effect on spirometry in asthmatic children and no changes in symptoms or spirometry were observed in healthy children. Thus, the effect of combined exposure to PM and gaseous co-pollutants appeared to have less effect on asthmatic children exposed under controlled laboratory conditions in comparison with field studies of children attending summer camp (Thurston et al., 1997). However, prior exposure to H_2SO_4 aerosol may enhance the subsequent response to ozone exposure (Linn et al., 1994; Frampton et al., 1995); the timing and sequence of the exposures may be important. Overall, the evidence suggests that the gaseous-particle interactions of ozone and acidity indicates are more likely to enhance the effects of PM exposures in children than adults, as children playing outdoors would tend to get higher exposures to these air pollution components (as opposed to adults indoors, where acidity and ozone exposure is diminished, relative to the outdoors).

While past acid aerosol research has focused largely on acidity in a particulate form (e.g., as $H_2SO_4^-$), recent research by Peters et al. (1999) as part of the Children's Health Study

raises the possibility that the acidity-particle interaction may extend to the interaction of vapor nitric acid (HNO_3) and particles. To study possible chronic respiratory effects of air pollutants, the authors initiated a 10-yr prospective cohort study of Southern California children, with a study design focused on four pollutants: ozone, particulate matter, nitric acid vapor, and nitrogen dioxide (NO_2). Twelve demographically similar communities were selected on the basis of historic monitoring information to represent extremes of exposure to one or more pollutants. In each community, about 150 public school students in grade 4, 75 in grade 7, and 75 in grade 10 were enrolled through their classrooms. Wheeze prevalence was positively associated with levels of both nitric acid (odds ratio [OR] = 1.45; 95% confidence interval [CI], 1.14-1.83) and NO_2 (OR = 1.54; 95% CI, 1.08-2.19) in boys (who usually spend more time outdoors than girls), and only nitric acid vapor was significant overall for boys and girls. The authors conclude, based on this cross-sectional assessment of questionnaire responses, that current levels of ambient air pollution in Southern California may be associated with effects on schoolchildren's respiratory morbidity. However, it seems unlikely that the highly water soluble HNO_3 could reach deep into the lungs without interaction with particles, much the way that SO_2 has been shown to be picked up by particles entering the lung (Amdur and Chen, 1989; Chen et al., 1992). Thus, it may be that there is a nitric acid-particle interaction that is underlying the nitric acid-child health effects associations reported by Peters and colleagues.

F. Implications of Health Effects Findings to the Adequacy of PM and Sulfate Standards

The health effects studies documented in this report provide substantial evidence that PM exposures at present ambient levels are adversely affecting the health of children in places throughout the world, including in California. However, whether a PM-health effects association is present or not at a given ambient level is difficult to determine from such studies because, when an effect is not found to be significant, it may be that there is merely insufficient power (e.g., too small a population, or too short a record period) to find an effect that may really be there. Also, such studies tend to be conducted on large populations, where the power is

greatest, but where concentrations are also usually highest (i.e., in cities), so studies of low levels are difficult to find. Thus, it is more challenging to evaluate at exactly what pollution exposure concentrations these documented health effects begin to occur for groups of susceptible individuals such as infants and children with asthma.

Probably the best database available at this time for the evaluation of the levels at which pollutants show significant adverse health effects is the body of medical visits and hospital admissions studies, as: 1) they represent a health effect outcome that is clearly adverse, with only long-term illness or death being worse, and; 2) they are reported in large enough numbers to provide sufficient statistical power, and are statistics that are routinely available for analysis, so there are a large number of studies available to evaluate, as documented in the above sections and Appendix A. Therefore, these studies will be examined here for insights into the adequacy of the present California standards for the protection of children's health.

The hospital admissions study most directly relevant to the question of the U.S. EPA's $PM_{2.5}$ standard's adequacy is that by Norris and colleagues (1999). As noted in Appendix A, the estimated mean $PM_{2.5}$ level (based upon nephelometry data) in that study of asthma hospital visits by Seattle children less than 18 was $PM_{2.5} = 12$ ug/m^3, and the PM association was still significant at these low levels, even after controlling for co-pollutants. This implies that the $PM_{2.5}$ annual average standard should be below 12 ug/m^3 if it is to protect children with asthma. The maximum $PM_{2.5}$ concentration was approximately 7 times this value, above the 65 ug/m^3 24-hr. maximum standard, but the $PM_{2.5}$ short-term standard is as a 3 year average, so that the standard may well also not have been exceeded at this location where acute effects have been documented. These results therefore indicate that the present Federal $PM_{2.5}$ annual standard is not sufficiently protective of children with asthma, and further suggest that the 24-hr maximum may also not be sufficiently protective.

However, the Morgan et al (1998) study of asthma hospital admissions in Sydney, Australia experienced a mean $PM_{2.5} = 9.6$ ug/m^3, but was unable to detect a significant $PM_{2.5}$ association, despite having larger daily counts and a longer record than the Norris et al (1999)

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study. This Australian study's results, when compared to the Norris and colleagues study results, suggests that the threshold of $PM_{2.5}$ mass effects on asthma admissions in children is approximately 10 ug/m^3 as an annual mean over several years.

Since the mean PM_{10} concentration during the Norris et al (1999) Seattle study was 21.7 ug/m^3, this study further indicates that the present California PM_{10} annual average standard (30 ug/m^3) is also not sufficiently protective. In the case of PM_{10}, this study's results are confirmed by other studies that have demonstrated significant associations at PM_{10} levels below 30 ug/m^3. As shown in Appendix A, Atkinson et al. (1999a,b) found significant associations with both children's respiratory emergency department (ED) visits and hospital admissions in London, England, where the mean PM_{10} = 28.5 ug/m^3. Similarly, Hajet confirms this result for London doctor's visits for asthma and lower respiratory disease in London, with a mean PM_{10} = 28.2 ug/m^3. Medina et al (1997) also finds significant associations between PM_{13} and doctor's house calls at PM_{13} mean = 25 ug/m^3. Since PM_{10} is a sub-component of PM_{13}, and will therefore average less than PM_{13}, this Paris study confirms the Norris et al. result that significant adverse health associations occur even at mean PM_{10} below 25 ug/m^3.

Given the results of Norris et al (1999) and confirming PM studies, it is clear that the sulfate standard of 25 ug/m^3 is far from sufficiently protective. The above sulfate health effects section made clear that sulfate is an especially potent component of $PM_{2.5}$, and it's annual average standard should therefore be even lower than that for $PM_{2.5}$. Available studies of sulfates and hospital admissions confirm this conclusion, including the above discussed Burnett (1994) study summarized in Table 6. The average Southern Ontario sulfate level (after eliminating sulfate artifact) was 5.3 ug/m^3, yet significant associations were found between sulfates and children's respiratory admissions, even after controlling for ozone. Analyses of respiratory admissions in Buffalo and New York City (Thurston et al., 1992) at mean levels of 9.3 and 8.9 ug/m^3, respectively, also find significant sulfate-respiratory associations at mean concentrations well below 25 ug/m^3. In addition, examination of the plot of the Ontario data from the Burnett et al. (1994) study (presented above in Figure 8) suggests that the sulfate threshold

of effects, if it exists, lies below 5 ug/m^3, perhaps at about 2 ug/m^3. Clearly, the existing California SO$_4$$^=$ standard is not now sufficiently stringent to protect public health.

G. Conclusions

Based upon the above facts and considerations, it is clear that significant adverse health effects can reasonably be expected to occur at present day ambient levels, especially among infants and children, based on the findings of published studies.

Among the factors that cause children to be especially affected by PM air pollution are:

- higher PM exposure concentrations due to greater PM personal cloud than adults;

- higher PM exposure patterns (e.g., more time spent outdoors and greater activity levels);

- higher doses per body weight and lung surface area;

- diminished pollution defenses in infants vs. older children and adults;

- PM exposures may adversely affect body (e.g., lung) development in children;

- higher prevalence of children with asthma than in other age groups,

- larger percentage of children made susceptible by poverty than other age groups; and,

- gas-particle interactions and particle-allergen interactions apparently make pollutants more toxic than they are alone, potentially making the individual pollutant standards not fully protective to susceptible populations, such as children.

Furthermore, an examination of key medical visits and hospital admissions studies conducted at relatively low ambient concentrations evaluated the adequacy of the existing Federal and California PM$_{10}$ and PM$_{2.5}$ mass and sulfate ambient air quality standards. It was found that these standards are not presently sufficiently protective of public health, since significant adverse health impacts have been documented in published studies to occur at ambient levels averaging well below these standards.

However, to help reduce any remaining uncertainties regarding the impacts of PM and sulfates on the health of infants and children, and to determine how to most optimally control such environmental insults, additional research is needed into many aspects of the PM-health effects association among children, including:

- improved identification of the specific characteristics of PM (e.g., ultrafines, acidity, elemental composition, etc.) that are contributing most to noted PM effects, and quantification of their relative roles in PM toxicity;

- further investigation as to whether acute exposures less than one day in length (e.g., 1-hour daily maximum), or longer multi-day exposures (e.g., 2 or more day average PM), also have health importance, over and above that captured by the 24-hour PM peak PM concentration measurement;

- further investigations into particle-gas and particle-allergen interactions;

- animal studies relating increased infection following particle exposure needed, as well as more epidemiological studies of respiratory infections in infants exposed to ambient particles.

- using both experimental and epidemiological methods, conduct further investigations of apparently larger effects of acute and long-term PM exposures on children, and especially infants.

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I. Appendix

**Recent Studies Evaluating PM Associations with Medical Visits
or Hospital Admissions in Infants and Children**

Table A-1. Summaries of Recently Published Acute PM-Medical Visits Studies of Children

Reference/Citation Location, Duration PM Index/Concentrations	Study Description:	Results and Comments	PM Index, Lag,, Excess Risk %, (95% CI=LCI-UCL), Co-Pollutants
Anderson, et al. (1998) London ('87-'92) Population = 7.2 MM BS daily mean = 14.6 ug/m^3 BS 25-75th IQR= 24-38	Poisson regression used to estimate the RR of London daily asthma hospital admissions associated with changes in O_3, SO_2, NO_2 and particles (BS) for all ages and for 0-14 (mean=19.5/d), 15-64 (mean=13.1/d) and 65+ years (mean =2.6/d).	O_3, SO_2, NO_2, and particles (BS) were all found to have associations with daily hospital admissions for asthma, but there was a lack of consistency across the age groups in the specific pollutant. The BS association was strongest in the 65+ group, especially in winter.	Asthma Admissions. BS=10 ug/m^3 BS Lag = 0-3 day average concentration All age ER= 2.3%(95%CI: 0.2-4.6%) <15yr. ER= 0.88%(95%CI:⁻1.8-3.7%) 15-64yr ER=0.47%(95%CI: 2.2-3.2%) 65+ yr. ER=8.6%(95%CI: 2.4-15.2%)
Atkinson et al. (1999a) London ('92-'94) Population = NR PM10 Mean = 28.5 ug/m^3 10th-90th IQR =15.8-46.5 ug/m^3 BS mean =12.7 ug/m^3 10th-90th IQR =5.5-21.6 ug/m^3	All-age Respiratory (mean=90/day), Asthma (25.9/day), and Other Respiratory (64.1/day) ED visits analyzed for associations with air pollutants using Poisson methods. Counts for ages 0-14, 15-64, and >64 also examined.	PM_{10} associated, but BS was not, for all-age/all-respiratory category. This may reflect higher toxicity by secondary particles vs. carbonaceous primary particles. PM_{10} results driven by significant children and young adult associations, while older adult visits had negative (but non-significant) PM_{10}-ED visit relationship.	PM_{10} (30.7 ug/m^3) No co-pollutant: All Respiratory ED visits All age(lag 1d)ER=3.0%(95%CI:0.8-5.2%) <15yrs(lag 2d)ER=3.9%(95%CI: 0.6-7.3%) 15-64yr(lag1d)ER=5.2%(95%CI:2.1-8.4%) Asthma ED visits All age(lag 1d)ER=5.4%(95%CI:1.8-9.0%) <15yrs (lag 2d)ER=7.4%(95%CI:2.1-13%) 15-64yr.(lg 1d)ER=7.8%(95%CI:2.8-13%)
Atkinson et al. (1999b) London ('92-'94) Population = 7.2 MM PM_{10} Mean = 28.5 ug/m^3 10th-90th IQR=15.8-46.5 ug/m^3 BS mean=12.7 ug/m^3 10th-90th IQR=5.5-21.6 ug/m^3	All-age Respiratory (mean=150.6/day), all-age Asthma (38.7/day), COPD plus Asthma in adults >64 (22.9/day), and lower Respiratory (64.1/day) in adults >64 (16.7/day) hospital admissions from London hospitals considered. Counts for ages 0-14, 15-64, and >64 also examined.	Positive associations were found between emergency hospital admissions for respiratory disease and PM_{10} and SO_2, but not for O_3 or BS. When SO_2 and PM_{10} were included simultaneously, the size and significance of each was reduced.	PM_{10} (30.7ug/m^3), no co-pollutant. All Respiratory Admissions: All age(lag 1d)ER=3.0%(95%CI:1.1-4.9%) 0-14 y (lag 1d)ER=4.9%(95%CI:2.1-7.7%) 15-64y(lag 2d)ER=4.2%(95%CI:2.6-7.3%) 65+ y.(lag 3d)ER=3.0%(95%CI:0.47-5.6%) Asthma Admissions: All age(lg 3d)ER=2.1%(95%CI:⁻1.1-5.4%) 0-14 y (lag 3d)ER=3.3%(95%CI:⁻0.7-7.5%) 15-64 y(lag 3d)ER=5.7%(95%CI:0.7-11.%) 65+ y.(lag 0d)ER=7.2%(95%CI:⁻1.25-16%)

Table A-1. Summaries of Recently Published Acute PM-Medical Visits Studies of Children

Reference/Citation Location, Duration PM Index/Concentrations	Study Description:	Results and Comments	PM Index, Lag,, Excess Risk %, (95% CI=LCI-UCL), Co-Pollutants
Braga et al.. (2000?) Author Affiliation: Non-Profit Research Funding: Public Sao Paulo, Brazil ('92-'93) Population = NR PM_{10} mean = 66.3 ug/m^3 PM_{10} Std. Deviation = 26.1 PM_{10} Min./Max. = 26.7/165.4	Pediatric (<13 yrs.) hospital admissions (mean=67.6/day) from public hospitals serving 40% of the population were regressed (using both Poisson and maximum likelihood methods) on pollutants, controlling for month of the year, day-of-week, weather, and the daily number of non-respiratory admissions (mean=120.7/day). Pollutants considered included PM_{10}, O_3, SO_2, CO, and NO_2.	PM_{10} and O_3 were the two pollutants found by the authors to exhibit the most robust associations with respiratory HA's. SO_2 showed no correlation at any lag. Simultaneous regression of respiratory HA's on PM_{10}, O_3, and CO decreased effect estimates and their significance, suggesting that "there may not be a predominance of any one pollutant over the others". No safe threshold was found for PM_{10} or O_3. Associations are ascribed primarily to auto emissions by the authors.	PM_{10} (66.3 ug/m^3), no-co-pollutant Respiratory Hospital Admissions (<13 yr.) (0-5 day lg avg.)ER=12%(95%CI:6.1-18%)
Delfino et al., 1997 Montreal,Canada (6-9/92,6-9/93) Population = 3 million 1993 Means (SD): PM_{10}= 21.7 ug/m^3 (10.2) $PM_{2.5}$= 12.2 ug/m^3 (7.1) $SO_4^=$= 34.8 nmol/m^3 (33.1) H^+= 4 nmol/m^3 (5.2)	Association of daily respiratory ED visits (mean = 98/day from 25 of 31 acute care hospitals) with O_3, PM_{10}, $PM_{2.5}$, $SO_4^=$, and H^+ assessed using linear regression with controls for temporal trends, auto-correlation, and weather. Five age sub-groups considered.	No associations with ED visits in '92, but 33% of the PM data missing then. In '93, only H^+ associated for children <2, despite very low H^+ levels. H^+ effect stable in multiple pollutant models and after excluding highest values. No associations for ED visits in persons 2-64 yrs. of age. For patients >64,O_3, PM_{10}, $PM_{2.5}$, and $SO_4^=$ were all positively associated with visits (p < 0.02), but PM effects smaller than for O_3.	Respiratory ED Visits Children <2 yrs: (H^+ lag = 2 day) 4 nmol/m^3 H^+ ER= 5.0% (CI = 0.4-9.6%) Adults >64: (pollutant lags = 1 day) 21.7 ug/m^3 PM_{10} ER= 16% (CI = 4-28%) 12.2 ug/m^3 $PM_{2.5}$ ER= 12% (CI = 2-21%) 34.8 nmol.m^3 $SO_4^=$ ER= 6% (CI = 1-12%)
Gouveia et al (2000) Author Affiliation: Non-profit Research Funding: Public Study Period.:'92-'94 Sao Paulo, Brazil Population = 9.5 MM x 66% PM_{10} mean = 64.9 ug/m^3 PM_{10} IQR = 42.9-75.5 ug/m^3 PM_{10}10/90th%ile=34.5/110ug/m^3 PM_{10} 95th%ile = 131.6 ug/m^3	Daily public hospital admissions for respiratory diseases by children (mean Resp. < 5y = 56.1/d; mean Pneumonia <5y =40.8/d; mean asthma <5 y = 8.5/d; mean Pneum.<1y=24.0) and daily levels of weather and air pollutants (PM_{10}, SO_2, NO_2, O_3, and CO) were analyzed with Poisson regression. PM_{10} measured by Beta-gauge.	Children's HA's for total respiratory and pneumonia gave positive associations with O_3, NO_2, and with PM_{10}. Effects for pneumonia greater than for all respiratory diseases. Effects on infants (<1 yr. old) gave higher estimates. Similar results for asthma, but estimates higher than for other causes. Results noted to agree with prior publications, but smaller RR's. This may be an artifact of higher baseline admission rates in this poor sub-population vs. other studies, but this is not intercompared by the authors.	For PM 10th-90th %ile =75.5 ug/m^3: All Respiratory HA's for children < 5yrs. ER = 4.0% (95% CI = $^-$1.5%, 9.9%) Pneumonia HA's for children <5 yrs. ER = 5.0% (95% CI = $^-$1.6%, 12.1%) Asthma HA's for children <5 yrs. ER = 5.2% (95% CI = $^-$7.7%, 19.8%) Asthma HA's for children <1 yrs. ER = 9.4% (95% CI = 1.3%, 18.0%)

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Hajet et al., 1999 London, England ('92'-'94) Population = 282,000 PM_{10} mean = 28.2 ug/m^3 PM_{10} 10^{t}-90th%=16.3-46.4 ug/m^3 BS mean = 10.1 ug/m^3 BS 10^{t}-90th%=4.5-15.9 ug/m^3	Examined associations of PM_{10}, BS, NO_2, O_3, SO_2, and CO, with primary care GP asthma and "other LRD" consultations [asthma means = 35.3 (all ages); = 14.(0-14 yrs,); = 17.7 (15-64 yrs.); = 3.6 (>64 yrs.)] [LRD means = 155. (all ages); = 39.7(0-14 yrs,); = 73.8 (15-64 yrs.); = 41.1 (>64 yrs.)], Time-series analyses of daily numbers of GP consultations were performed, controlling for time trends, season factors, day of week, influenza, weather, pollen levels, and serial correlation.	Positive associations, weakly significant and consistent across lags, were observed between asthma consultations and NO_2 and CO in children, and with PM_{10} in adults, and between other LRD consultations and SO_2 in children.. Across all of the various age, cause, and season categories considered in this research, PM_{10} was the pollutant most coherent in giving positive pollutant RR estimates for both asthma and other LRD (11 of 12 categories positive) in single pollutant models considered.	Asthma Doctor's Visits: 30 ug/m^3 PM_{10} (10-90th %ile Range) -Year-round, Single Pollutant: All ages (lg 2): ER=3.2% (CI=⁻0.4-6.8%) 0-14 yrs.(lg 1): ER=3.8% (CI=1.0-8.8%) 15-64 yrs.(lg 0): ER=5.4% (CI=1.6-9.2%) >64yrs.(lg 2): ER=7.1% (CI=⁻1.1-16%) Other Lower Resp. Dis. Doctor's Visits: 30 ug/m^3 PM_{10} (10-90th %ile Range) -Year-round, Single Pollutant: All ages (lg 2): ER=2.1% (CI=⁻0.4-3.8%) 0-14 yrs.(lg 1): ER=2.5% (CI=⁻0.7-5.8%) 15-64 yrs.(lg 2): ER=2.2% (CI=0.0-4.5%) >64yrs.(lg 2): ER=3.7% (CI=⁻0.3-7.2%)
Lin CA, et al, 2000 Author Affiliation: Non-profit Research Funding: NR Sao Paulo, BR ('91-'93) Population = NR PM_{10} mean =65 ug/m^3 PM_{10} SD = 27 ug/m^3 PM_{10} range = 15-193 ug/m^3	Respiratory ED visits by children (0-12 yrs.) to a major pediatric hospital (mean = 56/day) related to PM_{10}, SO_2, NO_2, CO, and O_3 using Gaussian linear regression modeling, Poisson modeling, and a polynomial distributed lag model. Lower Respiratory (mean = 8/day) and Upper Respiratory (mean = 39/day) ED visits, and visits due to Wheezing (mean=9/day), evaluated.	PM_{10} was found to be "the pollutant that exhibited the most robust and stable association with all categories of respiratory disease". O_3 was the only other pollutant that remained associated when other pollutants were all added to the model simultaneously. However, some pollutant coefficients went negative in multiple pollutant regressions, suggesting coefficient intercorrelations in the multiple pollutant models.	For 10 ug/m^3 PM_{10} (0-5 day lag mean) Respiratory ED Visits(<13 yrs.) Single Pollutant Model: PM_{10} ER=4.0% (CI=3.4%-4.6%) All-Pollutant Model: PM_{10} ER=5.2% (CI=4.0%-6.5%) Lower Respiratory ED Visits (<13 yrs.) Single Pollutant Model: PM_{10} ER=4.2% (CI=2.4%-6.0%) All-Pollutant Model: PM_{10} ER=8.0% (CI=5.0%-11%)
Medina et al., 1997 Greater Paris '91-'95 Population = 6.5 MM Mean PM_{13} = 25 ug/m^3 PM_{13} min/max = 6/95 ug/m^3 Mean BS = 21 ug/m^3 BS min/max = 3/130 ug/m^3	Evaluated short-term relationships between PM_{13} BS air pollution and doctors' house calls (mean=8/day; 20% of city total) in Greater Paris using Poisson regression.	A relationship between all age (0-64 yrs.) asthma house calls and PM_{13}, BS, SO_2, NO_2, and O_3 air pollution, especially for children aged 0-14 (mean = 2/day). In two-pollutant models including BS with, successively, SO_2, NO_2, and O_3, only BS and O_3 effects remained stable.	Doctor's Asthma House Visits: 10 to 50 ug/m^3 PM_{13}:5-95th%ile Increment Year-round, Single Pollutant: All ages (lg 2): ER=10% (CI=4-18%) 0-14 yrs.(lg 0-3): ER=32% (CI=16-51%) 15-64 yrs.(lg 2): ER=5% (CI=⁻5%-13%)

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Moolgavkar, et al (2000b) Author Affiliation: Non-profit Research Funding: Industry Study Period: 1987-1995 Los Angeles (LA County), CA Population = NR PM_{10} median = 44 ug/m^3 PM_{10} IQR= 33-59 ug/m^3 $PM_{2.5}$ median = 22 ug/m^3 $PM_{2.5}$ IQR = 15-31 ug/m^3	Investigated associations between air pollution and COPD HA's in LA, for children 0-19 (med.=17/d), adults 20-64 (med.=24/d), and adults 65+ (med. = 20/d). Used Poisson GAM's controlling for day-of-week, season, and splines of temperature and RH (but not their interaction) adjusted for overdispersion. Co-pollutants were O_3, SO_2, NO_2, and CO. PM data available only every 6th day, vs. every day for gases.	PM was associated with admissions in single pollutant models, but not in two pollutant models. Analysis in 3 age groups in LA yielded similar results. Author concludes that "the gases, other than ozone, were more strongly associated with COPD admissions than PM, and that there was considerable heterogeneity in the effects of individual pollutants in different geographic areas".	Most Significant Positive ER (t-statistic) Single Pollutant Models: LA COPD HA's (25 ug/m^3 PM_{10}, 10 ug/m^3 $PM_{2.5}$/$PM_{2.5-10}$) (0-19 yrs.): PM_{10} lg2=5.2% (t=3.4) (0-19 yrs.): $PM_{2.5}$ lg0=1.7% (t=1.9) (0-19 yrs.): $PM_{2.5-10}$ lg2=6.5% (t=4.3) (20-64 yrs.): PM_{10} lg2=3.2% (t=2.7) (20-64 yrs.): $PM_{2.5}$ lg2=2.2% (t=3.0) (20-64 yrs.): $PM_{2.5-10}$ lg2=3.5% (t=3.0) (>64 yrs.): $PM_{2.5-10}$ lg3=2.0% (t=1.8)
Morgan et al, 1998 Author Affiliation: Non-profit Research Funding: Public Sydney, AU ('90-'94) Population = NR $PM_{2.5}$ 24h. mean = 9.6 ug/m^3 $PM_{2.5}$ 10th-90th% =3.6-18 ug/m^3 $PM_{2.5}$ max-1h. mean=22.8ug/m^3 $PM_{2.5}$ 10th-90th%=7.5-44.4ug/m^3	A Poisson analysis, controlled for overdispersion and autocorrelation via GEE, of asthma (means: 0-14 yrs.=15.5/day; 15-64=9/day)), COPD (mean 65+yrs. =9.7/day), and heart disease HA's. $PM_{2.5}$ estimated from nephelometry. Season and weather controlled using dummy variables.	Childhood asthma was primarily associated with NO_2, while COPD was associated with both NO_2 and PM. 1-hr. max $PM_{2.5}$ more consistently positively related to respiratory HA's than 24-h avg $PM_{2.5}$. Adding all other pollutants lowered PM effect sizes, although pollutant inter-correlations makes many pollutant model interpretations difficult. No association found between asthma and O_3 or PM.	Asthma HA's Single Pollutant Model: For 24h $PM_{2.5}$ 10th-90th% =3.6-18 ug/m^3 1-14 yrs.(lag1) ER= -0.87%(CI=$^-$4.6 - 3.0) 15-64 yrs.(lag0) ER=1.31%(CI=$^-$2.3 - 5.1) For 1h $PM_{2.5}$ 10th-90th% =7.5-44.4 ug/m^3 1-14 yrs.(lag1) ER= -0.87%(CI=$^-$4.6 - 3.0) 15-64 yrs.(lag0) ER=1.31%(CI=$^-$2.3 - 5.1) Multiple Pollutant Model: For 24h $PM_{2.5}$ 10th-90th% =3.6-18 ug/m^3 1-14 yrs.(lag1) ER= -0.35%(CI=$^-$4.3 - 3.8)
Norris et al (1999) Author Affiliation: Non-profit Research Funding: Public Seattle, WA (9/95-12/96) Pop. Of Children <18= 107,816 PM_{10} mean. =21.7 ug/m^3 PM_{10} IQR = 11.6 ug/m^3 ϑ_{sp} mean = 0.4 m^{-1}/10^{-4} (12.0 ug/m^3 $PM_{2.5}$) ϑ_{sp} IQR = 0.3 m^{-1}/10^{-4} (9.5 ug/m^3 $PM_{2.5}$)	The association between air pollution and childhood (<18 yrs.) ED visits for asthma from the inner city area with high asthma hospitalization rates (0.8/day, 23/day/10K persons) compared with lower hospital use areas (1.1/day, 8/day/10K persons). Daily ED counts were regressed against PM_{10}, light scattering (ϑ_{sp}), CO, SO_2, and NO_2 using a semiparametric Poisson regression model evaluated for over-dispersion and auto-correlation.	Associations found between ED visits for asthma in children and fine PM and CO. CO and PM_{10} highly correlated with each other (r=.74) and K, an indicator of woodsmoke pollution. Considering baseline risks/10K population indicates a higher PM attributable risk (AR) in the inner city. These findings were seen even though the mean estimated $PM_{2.5}$ concentration was below the newly adopted annual National Ambient Air Quality Standard of 15 ug/m^3.	Children's (<18 yrs.) Asthma ED Visits Single Pollutant Models: For 24h PM_{10} IQR =11.6 ug/m^3 Lag1 ER= 14% (CI= 8% - 23%) For 24h ϑ_{sp} IQR =0.3 m^{-1}/10^{-4} (9.5 ug/m^3 $PM_{2.5}$) Lag1 ER= 15% (CI= 8% - 23%) Multiple Pollutant Models: For 24h PM_{10} IQR =11.6 ug/m^3 Lag1 ER= 14% (CI= 4% - 26%) For 24h ϑ_{sp} IQR=0.3 m^{-1}/10^{-4} (9.5 ug/m^3 $PM_{2.5}$) Lag1 ER= 17% (CI= 8% - 26%)

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Norris et al (2000) Author Affiliation: Non-profit Research Funding: Public Spokane, WA (1/95—3/97) Population = 300,000 PM_{10} mean. =27.9 ug/m³ PM_{10} Min/Max=4.7/186.4 ug/m³ PM_{10} IQR = 21.4 ug/m³ Seattle, WA (9/95—12/96) Pop. Of Children <18= 107,816 PM_{10} mean. =21.5 ug/m³ PM_{10} Min/Max = 8/69.3 ug/m³ PM_{10} IQR = 11.7 ug/m³	Associations investigated between an atmospheric stagnation index (# of hours below median wind speed), a "surrogate index of pollution", and asthma ED visits for persons <65 yrs. (mean=3.2) in Spokane and for children <18 (mean=1.8) in Seattle. Poisson GAM modeling, controlled for day of week, long-wave effects, and temperature and dew point (as non-linear smooths). Factor Analysis (FA) applied to identify PM components associated with asthma HA's.	Stagnation persistence index was strongly associated with ED visits for asthma in 2 cities. FA indicated that products of incomplete combustion (especially wood-smoke related K, OC, EC, and CO) are the air pollutants driving this association. Multi-pollutant models run with Stagnation as the "co-pollutant" indicated the importance of general air pollution over any single pollutant index, but provided no indication of the importance of the various pollutants relative to each other.	Asthma ED Visits Single Pollutant Models Persons<65 years (Spokane) For PM_{10} IQR = 21.4 ug/m³ Lag 3 ER = 1% (95% CI= ⁻5% - 7%) Persons<18 years (Seattle) For PM_{10} IQR = 11.7 ug/m³ Lag 3 ER = 11% (95% CI= 2% - 20%)
Ostro et al (1999) Author Affiliation: Non-profit Research Funding: World Bank Santiago, CI (7/92—12/93) <2 yrs. Population 20,800 3-14 yrs. Population 128,000 PM_{10} mean. =108.6 ug/m³ PM_{10} Min/Max=18.5/380 ug/m³ PM_{10} IQR = 70.3 – 135.5 ug/m³	Analysis of daily visits to primary health care clinics for upper or lower respiratory symptoms by children 2-14 years of age (mean LRS=111.1/day) and < age 2 (mean LRS=104.3/day). Daily PM_{10} and O_3 and meteorological variables considered. The multiple regression GAM included controls for seasonality (LOESS smooth), temperature, day of week, and month.	Analyses indicated an association between PM_{10} and medical visits for LRS in children ages 2-14 and in children under age 2. PM_{10} was not related to non-respiratory visits (mean =208/day). Results unchanged by eliminating high PM_{10} (>235 ug/m³) or coldest days (<8°C). Adding O_3 to the model had little effect on PM_{10}-LRS associations.	Lower Resp. Symptoms Clinic Visits PM_{10} IQR = 50 ug/m³, One Poll. Model: -Children<2 years Lag 3 ER = 2.5% (95% CI= 0.2% - 4.8%) -Children 2-14 years Lag 3 ER = 3.7% (95% CI=0.8% - 6.7%) Two Pollutant Models (with O_3): -Children<2 years Lag 3 ER = 2.2% (95% CI= 0% - 4.4%) -Children 2-14 years Lag 3 ER = 3.7% (95% CI=0.9% - 6.5%)
Rosas, et al (1998) Author Affiliation: Non-profit Research Funding: public SW Mexico City ('91) Population = NR PM_{10} mean. =77 ug/m³ PM_{10} min/max= 25/183 ug/m³	Log-regression analysis of the relationships between emergency admissions for asthma to a hospital for children <15 years (mean=2.5/day), adults (mean=3.0/day), and older adults >59 years (mean=0.65/day) and lag 0-2 average pollen, fungal spores, air pollutants (O_3, NO_2, SO_2, and PM_{10}) and weather factors. Long wave controlled only by separating the year into two seasons: "dry" and "wet". Day-of-week not included in models.	There were few statistical associations found between asthma admissions and air pollutant. Grass pollen was associated with child and adult admissions, and fungal spores were associated with child admissions. The authors conclude that aeroallergens may be more strongly associated with asthma than air pollutants, and may act as confounding factors in epidemiologic studies. Results are limited by low power and the lack of long-wave auto-correlation controls in the models.	NR

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Sunyer et al (1997) Barcelona ('86-'92) BS Median: 40 ug/m^3 BS Range: 11-258 (B Helsinki ('86-'92) BS Median: - BS Range: - Paris ('86-'92) BS Median: 28 ug/m^3 BS Range: 4-186 ug/m^3 London ('86-'92) BS Median: 13 ug/m^3 BS Range: 3-95 ug/m^3	Daily counts of asthma HA's and ED visits in adults [ages 15-64 years: mean/day = 3.9 (B); 0.7 (H); 13.1 (H); 7.3 (P)] and children [ages < 15 years: mean/day = 0.9 (H); 19.8 (L); 4.6 (P)] related to BS, SO$_2$, NO$_2$, and O$_3$ air pollution. Asthma (ICD9=493) studied in each city, but the outcome examined differed across cities:	In children, daily admissions increased significantly with SO$_2$ and positively (but non-significantly) with Black Smoke and NO$_2$, though the latter only in cold seasons. No association was observed in children for O$_3$. The weakness of PM in these analyses may be result of the use of the BS index, a measure of only the primary carbonaceous particles, which may be less toxic than other (i.e., secondary) aerosols.	ER per 50μg/m^3 BS (24 h Average) Asthma Admissions/Visits: <15 yrs.: London ER = 3.1% (lg 0d) Paris ER = 3.0% (lg 2d) Total ER = 3.0% (95%CI: ⁻2.1%-8.4%) 15-64 yrs: Barcelona ER = 3.6% (lg 3d) London ER = 3.5% (lg 0d) Paris ER = 1.2% (lg 0d) Total ER = 2.1% (95%CI: ⁻1.5%-5.9%)
Wong, et al (1999) Study Period.:'94-'95 Hong Kong Population = NR PM$_{10}$ mean = 50.1 ug/m^3 PM$_{10}$ median = 45.0 ug/m^3 PM$_{10}$ IQR = 30.7, 65.5 ug/m^3	Poisson regression applied to assess association of daily NO$_2$, SO$_2$, O$_3$, and PM$_{10}$ with emergency HA's for all respiratory (median = 131/day) and COPD (median = 101/day) causes. Effects by age groups (0-4, 5-64, and 65+ yrs.) also evaluated.	Positive associations were found for HA's for all respiratory diseases and COPD with all four pollutants. PM$_{10}$ results for lags 0-3 cumulative. Admissions for asthma, pneumonia, and influenza were associated with NO$_2$, O$_3$, and PM$_{10}$. Those aged > or = 65 years were at higher risk, except for PM$_{10}$.	PM$_{10}$ = 10 ug/m^3 (Lags = 0-3 days) Respiratory HA's All age: ER= 1.6% (95%CI: 1.0, 2.2%) 0-4yrs.: ER= 1.9% (95%CI: 1.1, 2.8%) 5-64yrs.: ER= 1.7% (95%CI: 0.9, 2.6%) 65+ yrs.: ER= 1.8% (95%CI: 1.0, 2.6%)